https://doi.org/10.17221/55/2021-VETMED

Benign ovarian teratoma in the dog with predominantly nervous tissue: A case report

*Peter Makovicky[1], Alexander Vladimirovic Makarevich[2], Pavol Makovicky[3], Alireza Seidavi[4], Luca Vannucci[5], Kvetoslava Rimarova[6]**

[1]*Infectious Diseases and Preventive Medicine, Veterinary Research Institute, v. v. i., Brno, Czech Republic*
[2]*National Agricultural and Food Centre, Research Institute for Animal Production, Lužianky, Slovak Republic*
[3]*Department of Biology, Faculty of Education, J. Selye University, Komárno, Slovak Republic*
[4]*Department of Animal Science, Rasht Branch, Islamic Azad University, Rasht, Iran*
[5]*Laboratory of Immunotherapy, Institute of Microbiology of the Czech Academy of Sciences, v. v. i., Prague, Czech Republic*
[6]*Department of Public Health and Hygiene, Faculty of Medicine, P. J. Šafárik University, Košice, Slovak republic*

**Corresponding author: kvetoslava.rimarova@upjs.sk*

Citation: Makovicky P, Makarevich AV, Makovicky P, Seidavi A, Vannucci L, Rimarova K (2022): Benign ovarian teratoma in the dog with predominantly neuronal tissue: A case report. Vet Med-Czech 67, 99–104.

Abstract: Ovarian teratomas are rare neoplasms in female dogs, and they are characterised by the proliferation of tissues of embryonic origin. Most teratomas are benign, but a histological diagnosis is important for clinicians. The objective of this article is to describe a benign ovarian teratoma in a dog, which was found on the street and was appearing like pregnant. A veterinary inspection by palpation documented an enlarged abdomen with a mass of tough matter located on the right side in the abdominal-pelvic part. An ultrasound examination presumed neoplastic mass in region of ovary. A bilateral ovariohysterectomy was performed and the subsequent histological evaluation revealed a benign ovarian teratoma with a histochemically and immunohistochemically verified nervous tissue. After one year, no distant metastases were found and the dog was recognised as being clinically healthy without problems. On the basis of the ultrasonography diagnostics and histopathological analyses, we have demonstrated the occurrence of a benign ovarian teratoma in a dog.

Keywords: germ cell neoplasm; ovary; veterinary pathology

Teratomas are neoplasms, "composed of abnormal tissue derived from at last two, and often all three, germinal layers. They presumably arise from pluripotent germ cells that undergone differentiation" (Linder et al. 1975). Ovarian teratomas are uncommon in domestic animals. They have been described most common in the bitch (Blaszak et al. 2009; Pegas et al. 2020). Histologically, benign and malignant forms are distinguishable. They are also classified as germ cell neoplasms that exhibit differentiation to mature tissues of the germ cell layers. There is some dispute about what classifies

Supported with grants KEGA of The Ministry of Education, Science, Research and Sport of the Slovak Republic (No. 007UPJŠ-4/2018, No. 008UPJŠ-4/2020, No. 010UPJŠ-4/2021) and internal grant of University of Pavol Jozef Safarik (No. IPEL VVGS-2020-1485).

https://doi.org/10.17221/55/2021-VETMED

a true teratoma. "Immature" refers to a neoplasm that is only comprised of embryonic tissue, with little to no differentiation to the fully developed tissue. Other classifications include the tissue arrangement (cystic, solid, mixed) and the grading. There are several reports documenting a teratoma's presence in dog ovaries (Gulcubuk et al. 2012; Yoshimura et al. 2017). Most of them are benign and composed of several tissue types. Even though the terms "immature" and "mature" have fallen out of favour, they are still used to distinguish between benign and malignant teratomas. In human medical pathology, a pre-pubertal and post-pubertal teratoma is the preferred definition. Benign ovarian teratomas composing of predominantly one tissue are less frequent. Nervous tissue is a usual part of benign ovarian teratomas, but there are not many reports documenting benign ovarian teratomas with predominantly neuronal tissue in dogs. On the other hand, neuronal tissue in a mature and immature human ovarian teratoma was documented by Chai et al. (2017) and Iemura et al. (2018). In this article, we describe the case of a dog with an ovarian benign teratoma composed of predominantly nervous tissue. This tissue was detected in all parts of the neoplasm subjected to the histological investigation, and the case was defined as a benign ovarian teratoma.

Case description

CLINICS

A dog, which was found on the street, was brought to the veterinary ambulance. It was a female crossbreed neglected dog, which was found on the street and appeared to be pregnant. A physical veterinary examination proved proved malnourished dog with an enlarged abdomen with a mass of tough matter localized on the right side in the abdominal-pelvic part. An ultrasound-guided (USG) investigation revealed an unbounded mass of the material and the finding was interpreted as a reproductive organ neoplasm. A supportive therapy was prescribed and a surgery was planned.

During the surgery, a massive neoplasm on the right ovary was found and a complete bilateral ovariohysterectomy was performed (Figure 1A–D). The post-surgical material was fixed in a 10% formalin solution and sent to the histopathological laboratory. The laboratory received the entire reproductive tract consisting of a part of the normally appearing vagina, uterus, left oviduct, left ovary and, on the right side, the massive neoplasm localised on the ovary.

MACROSCOPY

The observed structure on the ovary was defined as an ovoid neoplasm, approximately 25 × 20 × 10 cm in size. It appeared as an encapsulated mass of tissue consisting of several differently-sized cavities, filled by some serous fluid, which flowed after cutting. Part of the neoplasm (approximately ⅓) was calcified; the other part consisted of a mass of pale, soft and crumbling tissue with individual blood spaces (Figure 1E,F). Several samples from the different parts were taken for further histological investigation.

HISTOLOGICAL AND IMMUNOHISTOCHEMICAL ASSAYS

Selected samples were standardly processed and embedded into paraffin blocks. The samples were cut on a microtome and the sections were placed onto special slides (DAKO, Glosturp, Denmark). The first slices were stained with haematoxylin-eosin [(H&E); Bamed, s.r.o., České Budějovice, Czech Republic], the second slices were stained with periodic acid-Schiff [(PAS); Bamed, s.r.o., České Budějovice, Czech Republic] to detect the polysaccharides, then with a Masson trichrome (Bamed, s.r.o., České Budějovice, Czech Republic) to verify the collagen, and finally with Luxol fast blue (Bamed, s.r.o., České Budějovice, Czech Republic) to visualise the myelin. The other slices were processed for the immunohistochemistry with an anti-neurofilament (Zytomed Systems, Berlin, Germany) to visualise the neurofilaments, with an anti-GFAP (glial fibrillary acidic protein, RBK037; Zytomed Systems, Berlin, Germany) to visualise the nervous cells and finally with Ki-67 (DAKO, Glosturp, Denmark) to reveal the cell proliferation. Before the immunostaining, heat-induced antigen retrieval was performed by a 20 min treatment in a microwave, using a pH 6.0 retrieval buffer (target retrieval solution, high pH; DAKO, Glosturp, Denmark). Afterwards, the slices were incubated

https://doi.org/10.17221/55/2021-VETMED

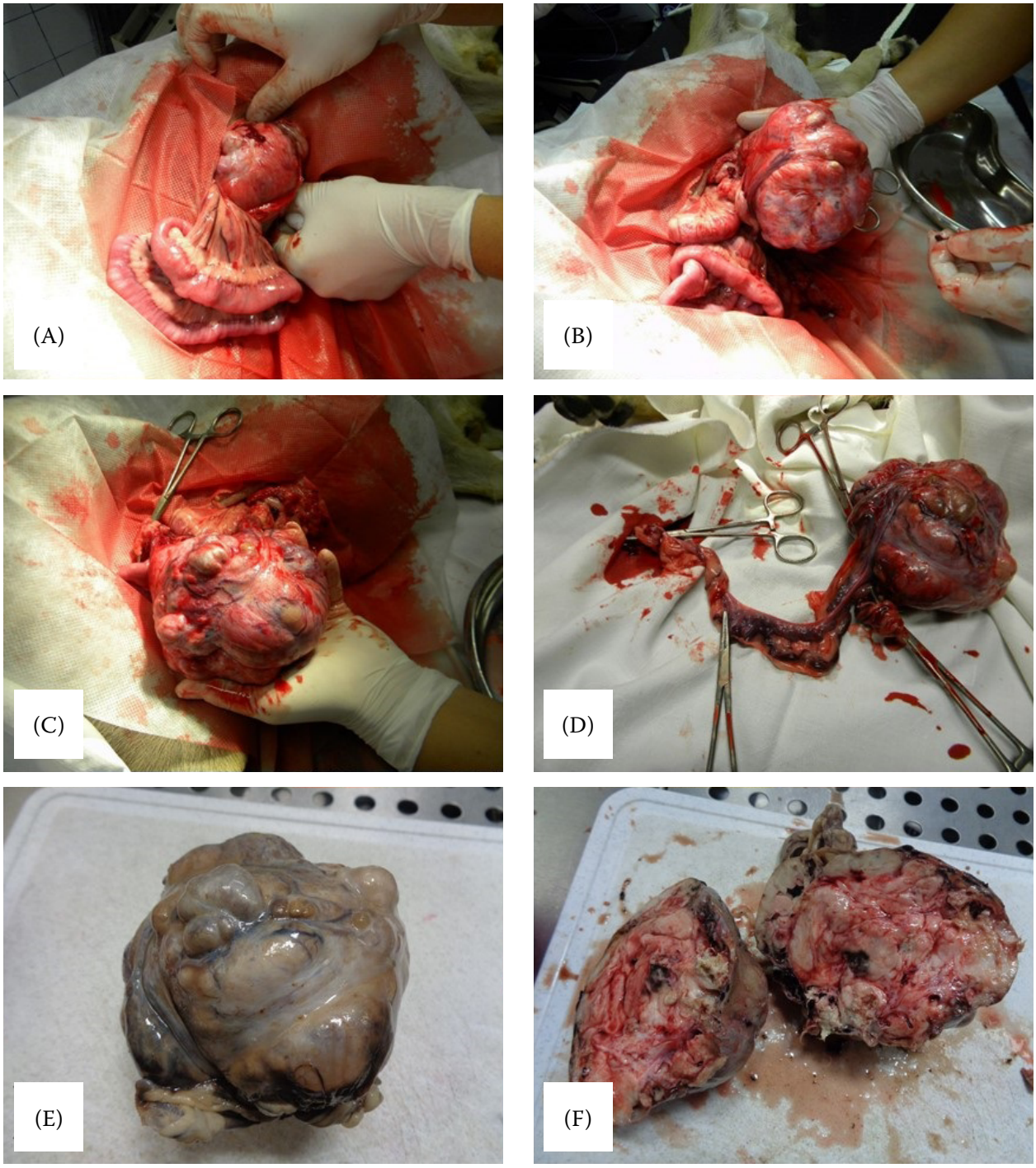

Figure 1. Macroscopy
(A–D) Macroscopic view to the neoplasm during surgery. (E, F) Macroscopic views to the tumour during trimming and sample selection for the histological processing

for 1 h at room temperature. For visualisation, an LSAB + System HRP kit (streptavidin-biotin peroxidase detection kit; DAKO, Glosturp, Denmark) was applied according to the product manual. The reaction was visualised with DAB + chromogen kit (Liquid DAB + Substrate Chromogen System; DAKO, Glosturp, Denmark). Finally, the slices were stained with Mayer haematoxylin (DiaPath, Martinengo, Italy). All the samples were analysed from the light microscope images obtained using an Olympus AX70 Provis microscope (Olympus, Tokyo, Japan).

https://doi.org/10.17221/55/2021-VETMED

RESULTS

The histological images are shown in Figure 2. Almost in the entire material there are alternating parts composed of completely differentiated nervous tissue containing diffusely arranged nervous (Figure 2A) and glial (Figure 2B) cells, which were located on the richly vascularised fine pinkish

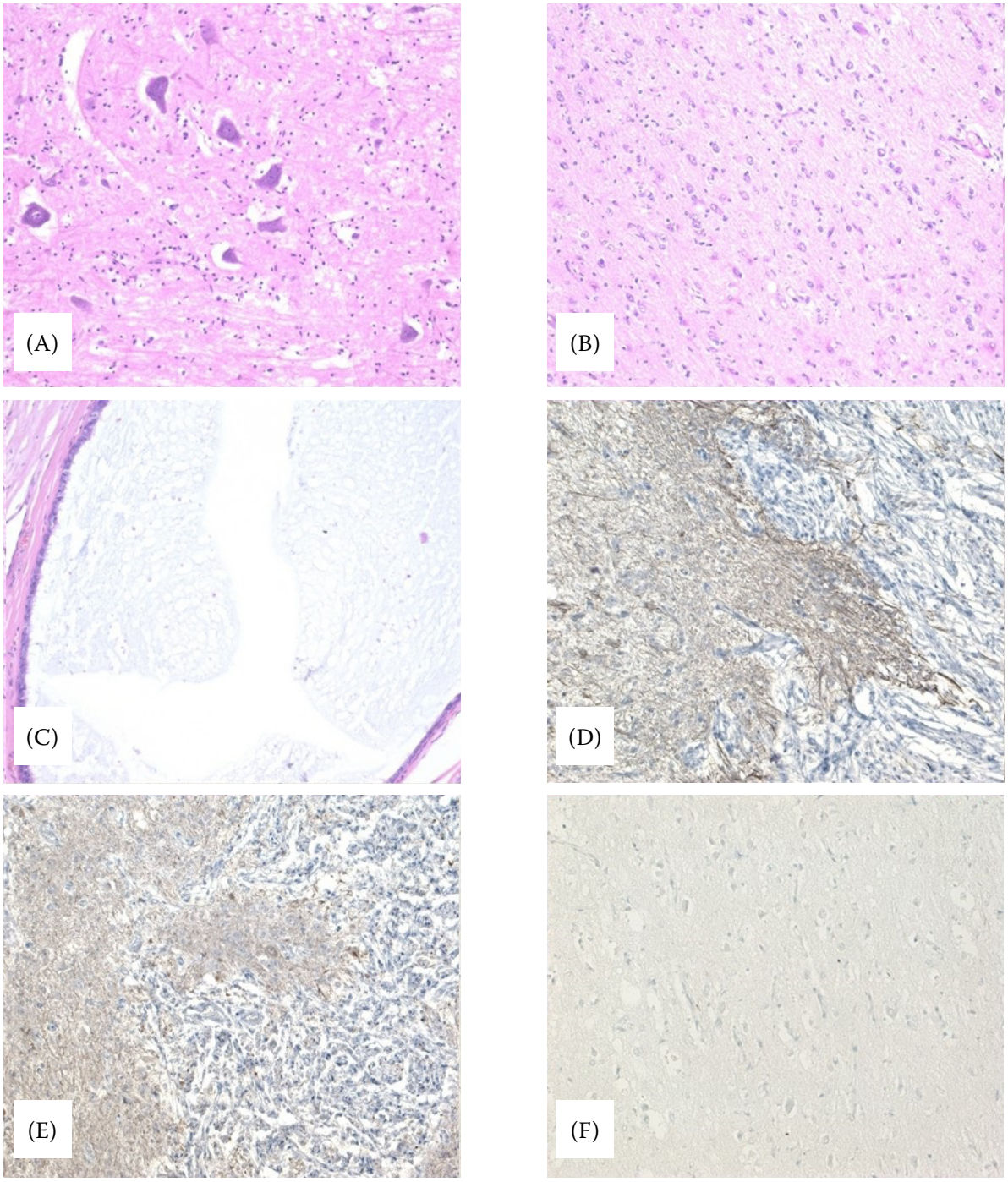

Figure 2. Histology and immunohistochemistry

(A) Histological image of the neoplasm consisting of nervous tissue with several well visible neuronal cells. H&E; × 200. (B) Well-developed nervous tissue in the entire sample. H&E; × 200. (C) Cyst formation, which is layered by a monolayer of epithelium resembling ependymal cells with superficially localised cilia. H&E; × 200. (D) GFAP-positivity in the neoplasm. GFAP; × 200. (E) Neurofilament-positivity in the neoplasm. Neurofilament; × 200. (F) Proliferation negativity in the neoplastic cells. Ki-67; × 200

https://doi.org/10.17221/55/2021-VETMED

vacuolated interstitial tissue. Part of the neoplasm was compressed, organised in shapeless, variable-sized nervous tissue nodules, which were separated by fibro-nervous septa containing spindle cells, resembling fibroblasts with some minimal collagenous fibres and some ovoid cells, resembling interstitial nervous cells. The complete finding was accompanied by several solid formations resembling peritoneal implants and isolated cystic structures, or only a remnant of rete ovarii, which were lined by a monolayer epithelium with superficially localised cilia formations (Figure 2C) resembling ependymal cells, including individual pigmented cells with some residual sparse serous secretion into the lumen. From place to place, there were some miniature shapeless structures corresponding to a differentiated hyaline cartilage and epidermoid cysts. The histochemical assay revealed a stromal Masson trichrome reaction, some isolated PAS positivity and Luxol fast blue negativity. Immunohistochemically, well visible GFAP positivity (Figure 2D) and neurofilament positivity (Figure 2E) in the nervous tissue and negative proliferation activity (Figure 2F) were observed in the neoplasm samples.

DISCUSSION AND CONCLUSIONS

Although canine teratomas are not a frequently occurring neoplasm, their benign variant is most often encountered. It is a germ cell neoplasm histologically composed of several tissues. The variety of tissues depends on the embryonic germ layers. A variety of tissue may be present including hair, bone, cartilage, teeth and the like. Most teratomas are benign and composed of well-differentiated mature tissues, but any of the tissue that make up a teratoma may be malignant (Nagashima et al. 2000; Yamaguchi et al. 2004; Xiang et al. 2018). Differential diagnosis should include dysgerminoma, sex cord stromal tumors, vascular hamartoma, fibroma, leiomyoma, rhabdomyosarcoma, as well as metastases from internal organs. However, the co-existence of an ovarian teratoma and uterine adenocarcinoma in a female dog was also reported (Pires et al. 2019).

Our case report shows that, in a neoplasm, one tissue can dominate over the others with a benign morphology. To the best of our knowledge, only one article with a similar finding in a dog was published thus far. Rota et al. (2013) described a dog with a mature ovarian teratoma consisting of highly differentiated nervous tissue, confirmed by the immunohistochemistry. On the other hand, there is an article describing an ovarian mature cystic teratoma in 25-year-old woman, which was mostly composed of neurogenic elements (Akbulut et al. 2006). This report documents that although benign teratomas contain variable tissues, they can be also monophasic. We suppose that benign teratoma always contains other tissues, which are not processed for histological investigation. Usually, these types of neoplasms grow into the largest size, creating a large abdominal mass of tissue, when a diagnostic imaging procedure is sufficient for the visualisation (Stussi et al. 2008). Although the enormous size of a benign teratoma with expansive growth and benign behaviour is evident without any clinical signs, several authors have documented that it can be malignant and have a metastasis potential (Coggeshall et al. 2012; Da Costa et al. 2017). For example, Patnaik and Greenlee (1987) found that 29% of canine ovarian neoplasms were metastasised; adenocarcinomas showed 48% metastases and malignant teratomas showed 50% metastases, and a distant metastasis was more common in a malignant teratoma. In dogs, it is assumed that one-third of teratomas are malignant having a metastatic potential and poor prognosis (De Bosschere et al. 1999). On the other hand, several cases showed no teratoma recurrence or other complications over years of follow up (Lopez et al. 2017; Sarrau 2018). This concurs with our finding.

Ultrasonography is a useful tool when examining intact bitches in diagnosing ovarian tumors such as teratomas, which have metastatic potential in some cases (Oviedo-Penata et al. 2020). Teratomas are tumours that have a higher prevalence in advanced age bitches, but in some cases, they can arise in younger animals. As it is documented in the above citations, they can occur and be diagnosed also in young women. This is probably in the context of prepubertal aggressive malignant tumours than of benign tumours arising in adulthoods. It is likely that gene mutations play here important role (Makovicky and Svecova 2016). This is in relationships with prognosis, including survival, age and can be applied also to teratomas.

On the basis of the USG diagnostics and histopathological analyses, we demonstrated the occurrence of benign ovarian teratoma, with prevalent nervous tissue, in a dog.

https://doi.org/10.17221/55/2021-VETMED

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

Akbulut M, Kelten EC, Ege CB. Mature cystic teratoma with predominantly neurogenic elements – Case report. Aegean Pathol J. 2006 Aug;22(3):18-20.

Blaszak B, Walkowski M, Ibbs M, Jaskowski JM. Teratoma adultum in a bitch: A case report. Vet Med-Czech. 2009 Aug;54(8):379-81.

Chai Y, Woo CG, Kim JY, Kim CJ, Khang SK, Kim J, Park IA, Kim EN, Kim KR. Diagnostic significance of cellular neuroglial tissue in ovarian immature teratoma. J Pathol Transl Med. 2017 Jan;51(1):49-55.

Coggeshall JD, Franks JN, Wilson DU, Wiley JP. Primary ovarian teratoma and GCT with intra-abdominal metastasis in a dog. J Am Anim Hosp Assoc. 2012 Nov-Dec;48 (6):424-8.

Da Costa DA, Da Silva MRM, De Souza NF, Pereira WLA, Cardoso AMC. Giant canine ovarian teratoma: Case report. J Cytol Histol. 2017 Aug;8(3):1-3.

De Bosschere H, Durnez V, Ducatelle R. Malignant ovarian teratoma in a Golden Retriever. Vlaams Diergeneesk Tijdcchr. 1999 Feb;68(2):96-100.

Gulcubuk A, Altun ED, Bozkurt ER, Sontas BS, Haktanir D. Ovarian teratoma in a dog. Turkish J Vet Anim Sci. 2012 May;36(5):573-6.

Iemura Y, Yamada Y, Hirata M, Kataoka TR, Minamiguchi S, Haga H. Histopathological characterization of the neuroglial tissue in ovarian teratoma associated with anti-N-methyl-D-aspartate (NMDA) receptor encephalitis. Pathol Int. 2018 Dec;68(12):677-84.

Linder D, McCaw BK, Hecht F. Parthenogenic origin of benign ovarian teratomas. N Engl J Med. 1975 Jan 9;292 (2):63-6.

Lopez D, Singh A, Wright TF, Gartley C, Walker M. Single incision laparoscopic-assisted ovariohysterectomy for an ovarian tumour in a dog. Can Vet J. 2017 Sep;58(9): 975-9.

Makovicky P, Svecova I. Veterinary pathology: The past, present and the future. Phenogenomic Newsletter. 2016 April;2(2):22-3.

Nagashima Y, Hoshi K, Tanaka R, Shibazaki A, Fujiwara K, Konno K, Machida N, Yamane Y. Ovarian and retroperitoneal teratomas in a dog. J Vet Med Sci. 2000 Jul;62 (7):793-5.

Oviedo-Penata CA, Hincapie L, Benavides CR, Maldonado JG. Concomitant presence of ovarian tumors (teratoma and granulosa cell tumor), and pyometra in an English Bulldog female dog: A case report. Front Vet Sci. 2020 Jan;14(6):500.

Patnaik AK, Greenlee PG. Canine ovarian neoplasms: A clinic-pathologic study of 71 cases, including histology of 12 granulosa cell tumors. Vet Pathol. 1987 Nov;24(6): 509-14.

Pegas GRA, Monteiro LN, Cassali GD. Extragonadal malignant teratoma in a dog – Case report. Arq Bras Med Vet Zootec. 2020 Jan-Feb;72(1):115-8.

Pires MDA, Catarino JC, Vilhena H, Faim S, Neves T, Freire A, Seixas F, Orge L, Payan-Carreira R. Co-existing monophasic teratoma and uterine adenocarcinoma in a female dog. Reprod Domest Anim. 2019 Jul;54(7):1044-9.

Rota A, Tursi M, Zabarino S, Appino S. Monophasic teratoma of the ovarian remnant in a bitch. Reprod Domest Anim. 2013 Apr;48(2):26-8.

Sarrau S. Iatrogenic ureteral lesion following a bulky ovarian teratoma excision in a 3-year bitch. Rev Veterinaire Clin. 2018 Apr;53(4):115-20.

Stussi A, Bohler A, Zednik T, Shiblz S, Zednik P. Teratoma – A rare ovarian tumour in a bitch. Wien Tierärztl Monatsschr. 2008 Mar;95(3):85-90.

Xiang H, Han J, Ridley WE, Ridley LJ. Canine tooth: Mature cystic teratoma. J Med Imaging Radiat Oncol. 2018 Oct; 62(S1):61.

Yamaguchi Y, Sato T, Shibuya H, Tsumagari S, Suzuki T. Ovarian teratoma with a formed lens and non-supportive inflammation in an old dog. J Vet Med Sci. 2004 Jul;66(7): 861-4.

Yoshimura, Yamamoto M, Moriya M, Endo T, Sugiura N, Kato T, Matsuda Y, Ishiwata T, Kajigaya H, Kamiiya S. Teratoma of the ovary in a free-ranging Japanese Raccoon dog (Nyctereutes Procyonoides Viverrinus). J Zoo Wildl Med. 2017 Mar;48(1):265-8.

Received: April 14, 2021
Accepted: September 22, 2021