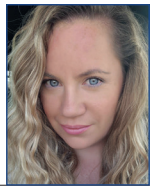
Testicular tumors in dogs



M. Efendić, D. Vnuk, L. Medven Zagradišnik, M. Hohšteter, J. Kuleš, A. Musulin and N. Maćešić*

Abstract

The aim of this research paper was to review the literature on testicular tumors in dogs, as the future of diagnostics and choice of therapy for oncological patients lies in tumor markers and proteomics research. Older dogs are prone to developing testicular tumors, which are usually benign, but in some cases can be malignant. The suspicion of a testicular tumor often arises incidentally during the clinical examination of a patient for another problem or during a systematic examination. It occurs most frequently in non-castrated individuals over the age of 10 years, and only very rarely do patients with testicular tumors show any symptoms. Histopathological examination is considered an objective diagnostic method for differentiating the types of testicular tumors in dogs. A testicular biopsy is also possible but does not guarantee a therapeutic effect. Histologically, testicular tumors in dogs are divided into germ cell tumors, testicular stromal tumors and mixed testicular tumors. Previous research determined serum and immunohistochemical markers for testicular tumors in dogs, and it has been found that there is a significant difference in the expression of anti-Müllerian hormone, testosterone and 17-beta-estradiol in the serum and tissue of testicular tumors in dogs, which is useful for diagnosis and treatment decisions. Recent research has focused on proteomics, which analyzes the entire protein component, and biomedical research has already begun to use it for diagnostic and prognostic markers of testicular tumors. To date, no proteomic studies have been performed on testicular tumors in dogs, but the expression of various proteins associated with oncogenic effects has been determined in dogs with different tumors compared to healthy dogs.

Key words: *canine testicular tumors; serum tumor markers; immunohistochemical tumor markers; proteomics*

Introduction

Testicular tumors in dogs are the most common type of tumor of the canine reproductive system and are among the top three most common tumor types after skin and fibrous tumors. Testicular tumors in dogs are usually not malignant (benign), but malignant changes do occur in some cases. Metastases most commonly affect the regional lymph nodes and the lungs, though the visceral organs can also be affected (Gopinath et al., 2009; Holst and Dremains, 2015; Mihoković et al., 2017).

The suspicion of a testicular tumor often arises incidentally during the clinical examination of a patient. It occurs most frequently in uncastrated individuals over 10 years of age, and very rarely do

Maša EFENDIĆ, Dražen VNUK, Lidija MEDVEN ZAGRADIŠNIK, Faculty of Veterinary Medicine, University of Zagreb, Zagreb, Croatia; Marko HOHŠTETER, Bioinstitute Čakovec, Čakovec, Croatia, Josipa KULEŠ, Andrija MUSULIN, (Corresponding author, e-mail: amusulin@vef.unizg.hr), Nino MAĆEŠIĆ, Faculty of Veterinary Medicine, University of Zagreb, Zagreb, Croatia

patients with testicular tumors show any symptoms (Gopinath et al., 2009; Liao et al., 2009; Efendić et al., 2021). In the expected clinical changes of the testis affected by the tumor, a change in consistency and sometimes also in the size of the testis can be observed, and when the ejaculate is evaluated, reduced and impaired spermatogenesis is possible (Camara et al., 2014; Holst and Dremains, 2015; Efendić et al., 2021). In advanced testicular tumor processes, hormonal disruption, i.e., hyperestrogenization, can occur, which can subsequently cause a dermatological clinical picture (bilateral symmetrical alopecia, hyperpigmentation at the site of alopecia with macular melanosis) and gynecomastia, non-regenerative normocytic normochromic anemia and hypoplasia of bone marrow can occur, but then the prognosis is unfavorable (Gopinath et al., 2009; Withers et al., 2016; Song et al., 2021). Hyperestrogenization has been described in Serttolli cell tumor (SCT), but cases have also been reported in dogs with seminoma (SEM) and Leydig cell tumor (LCT) (Peters et al., 2000; Gopinath et al., 2009; Hohšteter, 2012; Hitoshi et al., 2014; Song et al., 2021).

The increased prevalence of testicular tumors is associated with genetic factors, age, cryptorchidism, the external influence of carcinogenic properties and the predisposition of certain breeds (Liao et al., 2009; Hohšteter, 2012; Hitoshi et al., 2014; Holst and Dremains, 2015; Song et al., 2021; Efendić et al., 2021).

After clinical examination and the suspicion of a tumor process in the testicles, an ultrasound (US) examination of the testicles is indicated, which plays a key role in the detection of testicular tumors. In general, any vascularized mass that develops in the testis can be considered a tumor. There is no uniform morphological taxonomic system for describing testicular tumors in either human or veterinary medicine. In US examination, size, echogenicity, complexity, presence of solid and cystic components, margins and the presence of calcifications are observed. The complexity of the appearance of testicular tumors is multifactorial. Segmental infarcts, necrosis, hemorrhage, abscesses, hematomas, granulomatous and fibrotic areas, and calcifications can increase the morphological complexity of the tumor. Current guidelines for US imaging of the scrotum recommend the use of 7-15 MHz transducers, but ultra-wideband transducers in the 4-18 MHz range can also be used (Necas et al., 2021). Characterization of testicular morphology with US is difficult, therefore histopathology of testicular tissue is an important step in the final diagnosis of the type of testicular tumor (Mihoković et al., 2017; Hohšteter, 2012).

Histopathological confirmation takes place after the surgical procedure of orchiectomy, which is a diagnostic and therapeutic method. Histopathological examination is considered an objective diagnostic method for differentiating testicular tumor types in dogs (Mihoković et al., 2017). A testicular biopsy is also possible, but does not guarantee a therapeutic effect.

Histologically, testicular tumors in dogs are classified as:

1. *germ cell tumors* – seminomas histologically belongs to the mentioned tumor;
2. *gonadostromal /sex cord-stromal tumors* – Sertoli cell tumors (SCT) and Leydig cell tumors I(LCT) histologically belong to the mentioned tumor;
3. *mixed germ cell-sex cord stromal tumors*.

Testicular tumors in dogs most commonly occur as single tumors, though multiple tumors can also occur in one testicle. According to the World Health

Organization's classification of domestic animal tumors, the most common testicular tumors in dogs are testicular stromal tumors (spermatic cord tumors), germ cell tumors and mixed tumors. The most common subtypes of testicular tumors are LCT, SEM and SCT (Liao et al., 2009; Hohšteter, 2012; Hitoshi et al., 2014; Holst and Dremains, 2015; Song et al., 2021; Efendić et al., 2021).

1. Germ cell tumors

Germ cell tumors are usually not hormonally active, but if they develop a significant amount of placental tissue, they can secrete large amounts of human chorionic gonadotropin (hCG), a hormone that acts similarly to luteinizing hormone (LH). These tumors sometimes secrete estrogen hormones (Guyton and Hall, 2017). Germ cell tumors include seminomas (SEM), teratomas, embryonal carcinomas and yolk sac carcinomas. Of the above, only SEM is more common in pets, and teratomas are very rare (Hohšteter, 2012).

Seminomas often cause testicular enlargement, to a size of more than 6 cm. The enlargement and pain in the testicles are the result of intratubular hemorrhage and necrosis. Seminomas are usually soft in consistency, sometimes they can be hard, but to a lesser extent than in SCT. Histologically, they are divided into intratubular and diffuse forms. Microscopically, atrophic tubules are usually observed at the edge of the tumor, and occasionally accentuated intratubular spermatogonial proliferation can be seen in the altered testis. In humans, SEM are more common in younger men and are always considered malignant tumors, whereas in dogs they more often exhibit benign biological behavior, although metastases are more common in SEM than in SCT and LCT. The different biological behavior in humans and dogs is thought to be due to a different cellular origin. Histologically, seminomas are often locally invasive and tumor cells infiltrate the surrounding blood vessels or the tissue of the tunica albuginea, epididymis or spermatic cord, which is a clear criterion for malignancy. Metastases occur in dogs in less than 10% of cases (Hohšteter, 2012).

Teratomas are composed of several germ layers. They are extremely rare in dogs (Holst and Dremains, 2015), and in animals they occur more frequently in cryptorchid stallions between the first and fifth year of life, indicating the possibility of congenital development. The development of this tumor in the testis can result in the testis being unable to descend normally, and it can also lead to an enlargement of the testis. Their histological appearance varies. Testicular tissue with teratomas usually shows varying degrees of tubular atrophy and reduced spermatogenesis. In most cases, teratomas have a benign biological behavior, though they can also have malignant behavior (teratocarcinomas) (Hohšteter, 2012).

2. Gonadostromal /sex cord-stromal tumors

Sertoli cell tumors (SCT) and Leydig cell tumors (LCT) belong to this group. Sertoli cell tumors develop from the supporting cells of the seminiferous tubules. They are much harder in consistency than SEM or LCT. In 20% of cases, they are hormonally active, i.e., they can cause increased estrogen secretion and thus the occurrence of a feminization syndrome (Peters et al., 2000; Gopinath et al., 2009; Hohšteter, 2012; Hitoshi et al., 2014; Song et al., 2021). The symptoms of hyperestrogenization disappear after castration

if the tumor has not metastasized (Holst and Dremains, 2015). Microscopically, SCTs affect only the testis in most cases, but in malignant biological behavior they spread to neighboring structures of the tunica albuginea, epididymis or spermatic cord. Based on their histologic appearance, they are divided into intratubular and diffuse forms. Most SCTs are benign, but some 10-15% of tumors exhibit malignant biological behavior, and the incidence of metastases in tumors less than 2 cm is low. The biological behavior of diffuse histological forms is more often malignant, whereas intratubular forms are mostly benign. The prognosis in dogs with SCT is usually favorable if no metastases and/or bone marrow hypoplasia are present. If bone marrow hypoplasia occurs, the mortality rate is over 70% (Hohšteter, 2012).

Interstitial (Leydig) cell tumors arise from the interstitial cells of a normal testis and are histologically similar to them. There are reports that LCTs are associated with prostatic hyperplasia, prostate tumors, perineal hernias and perineal gland tumors. Despite the fact that the interstitial cells produce androgenic hormones and the tumor cells produce even greater amounts of these hormones, there is no evidence that these tumors lead to hyperandrogenism. In rare cases, these tumors cause a feminization syndrome. In ultrasound examination, a LCT can usually be recognized as well-circumscribed hypoechoic or hyperechoic areas. Due to their relatively small size (up to 2 cm), these tumors do not usually lead to an enlargement of the testicles, but can cause a change in the shape of the testicles, such as protrusions on the surface of small, soft and atrophic testicles. Histologically, they are well demarcated in cross-section, but are not or only very poorly encapsulated. Most interstitial tumors are biologically benign, although malignant forms (carcinoma of the interstitial cells) have also been described. Prognostically, castration leads to a favorable prognosis in most cases (Hohšteter, 2012).

3. Mixed germ cell-sex cord stromal tumors (MSCT)

To be histologically declared as MSCT, the tumor should meet the criteria of containing two or more tumor types that originate from stromal or interstitial tumors in a testis and consist of closely related germ and Sertoli cells, but not interstitial cells (Camara et al., 2014). These tumors are usually referred to as collision tumors, as they represent the junction of two different tumors in one testicle. Mixed tumor types exhibit features of SEM and SCT. The biological behavior is similar to SEM or SCT, and they usually do not lead to hyperestrogenism (Hohšteter, 2012).

Serological and immunohistochemical tumor markers

A neoplasm or a tumor produces substances called markers, *i.e.*, tumor markers. They can be determined in blood, body fluids or tissue, and certain types of tumor markers can be very specific for a given animal species. In healthy individuals, they are present in small amounts, while their concentrations increase with the appearance and growth of tumors. Due to the continuous progress of diagnostics in veterinary medicine, more and more emphasis is being placed on the diagnosis of tumors based on serological tumor markers. Also, immunohistochemical biomarkers have been determined for a range of tumors in dogs, including tes-

ticular tumors. Tumor markers are used as advanced diagnostics to detect tumors and/or to determine a specific therapy and to monitor the course of therapy. In veterinary medicine, the following tumor markers have been mentioned in connection with testicular tumors in dogs: most frequently anti-Müllerian hormone (AMH) and insulin-like factor 3 (INSL-3), while testosterone and 17-beta-estradiol are less present in the literature.

Anti-Müllerian hormone is a multifunctional cytokine, *i.e.*, a glycoprotein secreted by Sertoli cells in males and granulosa cells in females (Hitoshi et al., 2014; Walter, 2020). It belongs to the transforming growth factor beta (TGF-β) group, which regulates many aspects of physiological embryogenesis and tissue homeostasis and is involved in the pathophysiological mechanisms of many diseases (Tzavlaki and Moustakas, 2021).

In male dogs, AMH plays a role in inducing the regression of Müllerian ducts during embryogenesis, preventing the development of female genital organs. In male dogs, serum expression of AMH begins during fetal sexual differentiation and continues until puberty. In the post-pubertal phase of male mammals, AMH plays a role in the regulation of testosterone from Leydig cells (Banco et al., 2012; Hitoshi et al., 2014; Themmen et al., 2016).

Significant expression of AMH in serum was found in dogs with SCT (Hitoshi et al, 2014; Holst and Dremains, 2015) and in cryptorchid individuals, although the reason for the higher serum concentration of AMH in cryptorchids is thought to be due to an increased amount of immature Sertoli cells (Banco et al., 2012; Khan et al., 2018; Walter, 2020). A significantly lower serum AMH concentration was found in neutered individuals compared to non-neutered male and female dogs (Walter, 2020).

Based on previous studies, serum AMH has been found to be a good specific tumor marker for SCT, and a functional marker for the detection of a functional cryptorchid testis and for the differentiation of neutered individuals.

Alongside androsterone and dihydroandrosterone, testosterone is the most important natural androgen and is primarily a male sex hormone. In the testes and adrenal glands, androgens can be synthesized from cholesterol or directly from acetyl-coenzyme A (Samardžija et al., 2018). A reduced serum testosterone concentration is expected in dogs with SCT. Feminization syndrome in dogs has been found to be associated with a decrease in the ratio of serum estradiol to testosterone below the reference value (Mischke et al., 2002; Gopinath et al., 2009). Testosterone has been shown to have a lower serum level in cryptorchid dogs (Hornakova et al., 2017). A negative correlation was also found between testosterone and AMH in males, as testosterone suppresses the production of AMH from Sertoli cells (Themmen et al., 2016).

The hormone 17-beta-estradiol has proved to be a useful serum marker in the differentiation of cryptorchidism, as it is also elevated in cryptorchid dogs (Hornakova et al., 2017), just as estradiol was elevated in dogs with SCT and showed a significantly high concentration in dogs with feminization syndrome (Peters et al., 2000; Mischke, 2012; Hitoshi et al., 2014; Withers et al., 2016).

The expression of INSL-3 in serum is associated with cryptorchidism, where its level is significantly lower (Hohšteter, 2012).

Certain immunohistochemical markers (biomarkers) are used to differentiate human testicular tumors, and some of them have also been studied in dogs with

testicular tumors, such as AMH, Ki-67, INSL-3, alpha-fetoprotein, lactate dehydrogenase, c-KIT , CD-30, TERT, PCNA, p53, E-cadherin, GATA-4, cytokeratin, inhibin-α, OCT3/4, PGP 9.5, desmin and vimentin (Papaioannou et al., 2009; Banco et al., 2012; Hohšteter, 2012; Hohšteter et al., 2014; Posastiuc et al., 2022).

In veterinary medicine, there are only a few studies on the immunohistochemical expression of AMH in dogs with testicular tumors. It has been found that fetuses, neonatal puppies, and puppies up to 45 days of age have immunohistochemical expression of AMH, while older puppies and adults do not have significant expression of AMH. Dogs with SCT show significant immunohistochemical expression of AMH, indicating that AMH is a useful marker for immature and tumorous Sertoli cells in dogs (Banco et al., 2012).

The monoclonal antibody Ki-67 is a nuclear protein that is a good indicator of tumor cell proliferation by immunohistochemical methods, which is why it is often referred to as a proliferation marker. It is commonly used in medicine to detect expression in breast cancer in women to assess tumor grade by histopathological analysis (Plavetić et al., 2013). It has been found that in dogs with SEM, as more than 50% of SEM cells express Ki-67 and calretinin antibodies (Hohšteter, 2012).

Sertoli cells are the only testicular cells whose cytoplasm is immunohistochemically extremely positive for neuron-specific enolase and also diffusely stained with vimentin.

Studies on cytokeratin in veterinary medicine show that there is no immunoreactivity for cytokeratin in SEM, whereas the detected expression is most frequently found in SCT and mixed SCT tumors and rarely in LCT. Cytokeratin has been shown to be a good biomarker for the differentiation of testicular stromal tumors and testicular germ cell tumors.

Germ cell tumors, i.e., in SEM, c-KIT showed positive immunohistochemical expression, and the biomarker PLAP also showed positive immunohistochemical expression in SEM in dogs (Hohšteter, 2012; Hohšteter et al., 2014).

Proteomic research

In biomedicine, proteomics is already extremely useful for finding new tumor markers. Proteomics deals with the study of proteins and enables their identification and quantification in cells, tissues, and biological fluids as well as the analysis of changes in protein expression in healthy and diseased cells. Accordingly, the future of diagnostics and the choice of therapy for oncological patients also lies in proteome research (Graves and Haystead, 2002; Aebersold and Mann, 2003; Bilić et al., 2018; Kuleš et al., 2021; Šimonji, 2023). Numerous proteomic and genomic data sets of mammals are already available in publicly accessible databases, but there are currently no data on proteomic studies of testicular tumors in dogs in the available literature.

Conclusions

From the reviewed literature, it appears that this area is not well researched, particularly in terms of proteomic research on testicular tumors in dogs. Testicular tumors are the most common type of tumor of the canine reproductive system and are usually not malignant. Histopathological examination is considered an objective diagnostic method for differentiating testicular tumor types in dogs. In veterinary medicine, the following tumor markers have been mentioned in connection with testicular tumors in

dogs: AMH, INSL-3, testosterone and 17-beta-estradiol, Ki-67. The future of diagnostics and choice of therapy for oncologic patients lies in proteomic research.

References

1. AEBERSOLD, R. and M. MANN (2003): Mass spectrometry-based proteomics. Nature 422, 198-207. 10.1038/nature01511. 10.1038/nature01511
2. BANCO, B., M. C. VERONESI, C. GIUDICE, A. ROTA and V. GRIECO (2012): Immunohistochemical Evaluation of the Expression of Anti-Müllerian Hormone in Mature, Immature and Neoplastic Canine Sertoli Cells. J. Comp. Pathol. 146, 18-23. 10.1016/j.jcpa.2011.03.011
3. BILIĆ, P., J. KULEŠ, A. GALAN, L. GOMES DE PONTES, N. GUILLEMIN, A. HORVATIĆ, A. FESTA SABES, V. MRLJAK and P. D. ECKERSALL (2018): Proteomics in Veterinary Medicine and Animal Science: Neglected Scientific Opportunities with Immediate Impact. Proteomics 18. 10.1002/pmic.201800047. 10.1002/pmic.201800047
4. CAMARA, L. B. R. M., D. R. CÂMARA, F. C. MAIORION, V. A. SILVA JÚNIOR and M. M. P. GUERRA (2014): Canine testicular disorders and their influence on sperm morphology. Anim. Reprod. 11, 32-36.
5. DEDIĆ PLAVETIĆ, N., J. JAKIĆ- RAZUMOVIĆ, M. BARIĆ, A. KULIĆ, M. SIROTKOVIĆ- SKERLEV and D. VRBANEC (2013): Prognostička vrijednost ki-67 u karcinomima dojke: usporedba metode tkivnog mikropostroja s metodom analize cijelog reza. 6. Simpozij i godišnji sastanak Hrvatskog društva za internističku onkologiju HLZ-a, 7. - 11. studeni, Zagreb, 64.
6. EFENDIĆ, M. N. MAĆEŠIĆ, T. KARADJOLE, et al. (2021): Incidence of testicular tumors in dogs undergoing elective orchidectomy. 9th International Congress Veterinary Science and Profession, October, 9th, Zagreb, 97.
7. GOPINATH, D., D. DRAFFAN, A. W. PHILBEY and R. BELL (2009): Use of intralesional oestradiol concentration to identify a functional pulmonary metastasis of canine sertoli cell tumour. J. Small Anim. Pract. 50, 198-200. 10.1111/j.1748-5827.2008.00671.x
8. GRAVES, P. R. and T.A. HAYSTEAD (2002): Molecular biologist's guide to proteomics. Microbiol. Mol. Biol. Rev. 66, 39-63. 10.1128/MMBR.66.1.39-63.2002
9. GUYTON, A. C. and J. E. HALL (2017): Medicinska fiziologija. Medicinska naklada, Zagreb, 13. Izdanje.
10. HITOSHI, A., Y. HIDAKA and H. KATAMOTO (2014): Evaluation of anti-Müllerian hormone in a dog with a Sertoli cell tumour. Vet. Dermatol. 25, 142-145. 10.1111/vde.12112
11. HOHŠTETER, M. (2012): Poredbena patologija tumora sjemenika psa i čovjeka u Republici Hrvatskoj. Disertacija, Sveučilište u Zagrebu, Veterinarski fakultet, Sveučilišta u Zagrebu, Zagreb, Hrvatska.
12. HOHŠTETER, M., B. ARTUKOVIĆ, K. SEVERIN, A. GUDAN KURILJ, A. BECK, I.-C. ŠOŠTARIĆ-ZUCKERMANN and Ž. BRABAREVIĆ (2014): Canine testicular tumors: two types of seminomas can be differentiated by immunohistochemistry. BMC Vet. Res. 10, 169. 10.1186/s12917-014-0169-8
13. HOLST, B. S. and U. DREIMAINS (2015): Anti-Müllerian hormone: a potentially useful biomarker for the diagnosis of canine Sertoli cell tumours. BMC Vet. Res. 11, 166. 10.1186/s12917-015-0487-5
14. HORNAKOVA, L., T. VRBOVSKA, M. PAVL'AK, A. VALENCAKOVA-AGYAGOSOVA, M. HALO and J. HAJURKA (2017): The evaluation of blood concentrations of testosterone, 17β-oestradiol and anti-Müllerian hormone in dogs with cryptorchidism and testicular tumours. Pol. J. Vet. Sci. 20, 677-685.
15. KHAN, F. A., C. J. GARTLEY and A. KHANAM (2018): Canine cryptorchidism: An update. Reprod. Domest. Anim. 53, 1263-1270. 10.1111/rda.13231
16. KULEŠ, J., L. LOVRIĆ, A. GELEMANOVIĆ, B. BEER LJUBIĆ, I. RUBIĆ, M. BUJANIĆ and D. KONJEVIĆ (2021): Complementary liver and serum protein profile in wild boars infected by the giant liver fluke Fascioloides magna using tandem mass tags quantitative approach. J. Proteomics 247, 104332. 10.1016/j.jprot.2021.104332
17. LIAO, A. T., P.-Y. CHU, L.-S. YEH and C.-H. LIU (2009): A 12-Year Retrospective Study of Canine Testicular Tumors. J. Vet. Med. Sci. 71, 919-923. 10.1292/jvms.71.919
18. MIHOKOVIĆ, S. D. KNEZIĆ, M. MIŠIĆ, M. POPOVIĆ and M. HOHŠTETER (2017): Komparativna analiza tumora sjemenika pasa upotrebom histopatološke pretrage i metodom protočne citometrije. Veterinar 55, 2-8.
19. MISCHKE, R., D. MEURER, H.-O. HOPPEN, S. UEBERSCHÄR and M. HEWICKER- TRAUTWEIN (2002): Blood plasma concentrations of oestradiol-17b, testosterone and testosterone/oestradiol ratio in dogs with neoplastic and degenerative testicular diseases. Res. Vet. Sci. 73, 267-272. 10.1016/S0034-5288(02)00100-5
20. NECAS, M., M. MUTHUPALANIAPPAAN and C. BARNARD (2021): Ultrasound morphological patterns of testicular tumours, correlation with histopathology. J. Med. Radiat. Sci. 68, 21-27. 10.1002/jmrs.426
21. PAPAIOANNOU, N., D. PSALLA, M. ZAVLARIS, P. LOUKOPOULOS, N. TZIRIS and I. VLEMMAS (2009): Immunohistochemical expression of dogTERT in canine testicular tumours in relation to PCNA, ki67 and p53 expression. Vet. Res. Commun. 33, 905-919. 10.1007/s11259-009-9308-2
22. PETERS, M. A. J., F. H. DE JONG, K. J. TEERDS, D. G. DE ROOIJ, S. J. DIELEMAN and F. J. VAN SLUIJS (2000): Ageing, testicular tumours and the pituitary-testis axis in dogs. J. Endocrinol. 166, 153-161. 10.1677/joe.0.1660153

23. POSASTIUC, F. P., A. I. DIACONESCU, N. T. CONSTANTIN, C. MICŞA and M. CODREANU (2022): Potential biomarkers for testicular cancer in dogs - groundwork for innovative screening programs: a review. Scientific Works. Series C. Vet. Med. 68, 100-107.
24. SAMARDŽIJA, M., T. MAGAŠ, L. RADMANIĆ and J. PLEADIN (2018): The use of testosterone in domestic animals - therapeutic and anabolic activities. Vet. stn. 49, 287-296. (In Croatian).
25. SONG, D.-W., C.-M. LEE, S.-G. KIM, M.-H. KANG, D.-W. KIM, H.-Y. KIM, K. EOM and H.-M. PARK (2021): Testosterone/Estradiol Ratio in a Dog with Sertoli Cell Tumor-Seminoma Combination. J. Vet. Clin. 38, 221-224. 10.17555/jvc.2021.38.5.221
26. ŠIMONJI, K. (2023): Proteomsko profiliranje seruma i jetre jelena običnog (cervus elaphus) primjenom spektrometrije masa. Disertacija, Sveučilište u Zagrebu, Veterinarski fakultet, Sveučilišta u Zagrebu, Zagreb, Hrvatska.
27. THEMMEN, A. P. N., B. KALRA, J. A. VISSER, A. KUMAR, G. SAVJANI, J. DE GIER and S. JAQUES (2016): The use of anti-Müllerian hormone as diagnostic for gonadectomy status in dogs. Theriogenology 86, 14667-14747. 10.1016/j.theriogenology.2016.05.004
28. TZAVLAKI, K. and A. MOUSTAKAS (2020): TGF-β Signaling. Biomolecules 10, 487. 10.3390/biom10030487
29. WALTER, B. (2020): Anti-Müllerian hormone in dogs and cats reproduction. Reprod. Domest, Anim. 55 (S2), 26-31. 10.1111/rda.13603
30. WITHERS, S. C. M. LAWSON, A. G. BURTON, R. B. REBHUN and M. A. STEFFEY (2016): Management of an invasive and metastatic Sertoli cell tumor with associated myelotoxicosis in a dog. Can. Vet. J. 57, 299-304.

Tumori testisa u pasa

Maša EFENDIĆ, Dražen VNUK, Lidija MEDVEN ZAGRADIŠNIK, Veterinarski fakultet Sveučilšta u Zagrebu, Zagreb, Hrvatska; Marko HOHŠTETER, Bioinstitut Čakovec, Čakovec, Hrvatska, Josipa KULEŠ, Andrija MUSULIN, Nino MAĆEŠIĆ, Veterinarski fakultet Sveučilišta u Zagrebu, Zagreb, Hrvatska

Cilj je ovog istraživanja pregled literature o tumorima testisa u pasa, budući da je budućnost dijagnostike i izbora terapije onkoloških bolesnika u istraživanju tumorskih markera i proteomici. Stariji su psi skloni razvoju tumora testisa koje su, najčešće, dobroćudne prirode, no u nekim slučajevima dolazi i do zloćudnog biološkog ponašanja. Postavljanje sumnje na tumor testisa često se događa slučajno prilikom kliničkog pregleda pacijenta zbog drugih simptoma ili prilikom sistematskog pregleda. Vrlo rijetko pacijenti s tumorom testisa pokazuju bilo kakve ikakve simptome i najčešće se javlja u nekastriranih jedinki starijih od 10 godina, Smatra se da je histopatološka pretraga objektivna dijagnostička metoda za razlikovanje tipova tumora testisa u pasa. Biopsija testisa je moguća, ali time nije osiguran i terapijski učinak. Histološki, tumori testisa u pasa klasificiraju se kao tumori zametnih stanica, tumori strome testisa i mješoviti tumori testisa. Dosadašnjim istraživanjima utvrđeni su serumski i imunohistokemijski markeri za tumore testisa u pasa i time je utvrđeno da postoji značajna razlika u ekspresiji anti-Müllerovog hormona, testosterona i 17-beta estradiola u serumu i tkivu tumorskih testisa u pasa što je korisno u svrhu postavljanja dijagnoze i odluke o terapiji. Novija istraživanja stavljaju naglasak na proteomiku koja analizira kompletnu proteinsku komponentu, a u biomedicini se već počela koristiti u svrhu dijagnostičkih i prognostičkih markera tumora testisa. Do sada nisu provedena proteomska istraživanja na tumorima testisa u pasa, no utvrđena je ekspresija različitih proteina povezanih s onkogenim učinkom u pasa s različitim tumorima u odnosu na zdrave pse.

Ključne riječi: *tumori testisa pasa, serumski tumorski markeri, imunohistokemijski tumorski markeri, proteomika*