

Transmissible venereal tumor (TVT) metastatic in a bitch: case report

Tumor venéreo transmissível (TVT) metastático em cadela: relato de caso

Pietra Malu Franzener Detoni^{1*}, Vinicius Dahm¹, Amália Ferronato¹, Crisan Smaniotto¹, Arthur Colombari Cheng², Lorena Santos Pinheiro¹, Camila Campagnolo¹, Aline de Marco Viott¹

ABSTRACT

The canine transmissible venereal tumor is one of the most common neoplasms mainly in stray dogs, being classified morphologically as a round cell neoplasm. The present work aims to report a case of metastatic transmissible venereal tumor (TVT) in an adult mongrel bitch (SRD). In the necroscopic evaluation, the presence of neoformations in the vulva/vagina, spleen and parietal pleura was observed, in which all exhibited the same macroscopic characteristics. To elucidate the case, cytological and histological examinations were performed, in which similar morphological patterns were observed in the three analyzed tissues, being compatible with TVT. Metastasis is uncommon in this type of neoplasm, although reports are found in the literature showing the TVT's metastatic ability, the occurrence is more frequent in immunosuppressed animals, and the main tissues affected are the regional lymph nodes. However, cavitory organs can also be sites of metastasis, as observed in the present case. Although rare, it is concluded that metastases can occur and the importance of including TVT as a differential diagnosis of intracavitary neoplasms is highlighted.

Keywords: Dog. Metastasis. Round cell tumor. Thorax.

RESUMO

O tumor venéreo transmissível canino é uma das neoplasias mais comuns principalmente em cães errantes, sendo classificado morfológicamente como uma neoplasia de células redondas. O presente trabalho tem por objetivo relatar um caso de tumor venéreo transmissível (TVT) metastático em uma cadela adulta sem raça definida (SRD). Na avaliação necroscópica, verificou-se a presença de neoformações na vulva/vagina, no baço e na pleura parietal, nas quais todas exibiam as mesmas características macroscópicas. Para elucidação do caso, realizaram-se exames citológicos e histológicos, com o intuito de observar padrões morfológicos semelhantes nos três tecidos analisados, sendo compatíveis com TVT. A metastização é uma complicação incomum nesse tipo de neoplasma, embora na literatura sejam encontrados relatos evidenciando a capacidade metastática do TVT, a ocorrência é com maior frequência em animais imunossuprimidos e os principais tecidos acometidos são os linfonodos regionais. Os órgãos cavitários, entretanto, também podem ser sítios de metástase, conforme averiguado no presente caso. Embora sejam raras, conclui-se que as metastizações podem ocorrer e realça-se a importância da inclusão do TVT como diagnóstico diferencial de neoplasias intracavitárias.

Palavras-chave: Cão. Metástase. Tórax. Tumor de células redondas.

¹Federal University of Parana – UFPR, Palotina, PR, Brazil.

²Auburn University, Auburn, Alabama, EUA.

*pietradetoni@gmail.com

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INTRODUCTION

The canine transmissible venereal tumor (TVT) is a round cell neoplasm that has no sexual breed, or age predisposition, involving especially the external genital organs (Solano-Gallego & Masserdotti, 2023). Because it is a transmissible neoplasm, direct contact is pointed out as an extremely important factor for the appearance of the neoplasm, mainly through licking or sexual contact. (Pimentel, Oliveira & Horta, 2021).

Despite genital occurrence being the most frequent, extragenital manifestations are also reported in the literature, occurring mainly in the skin, nasal plane, eyes and oral mucosa (Zupa, Oliveira, Theodoro & Lúcio, 2019; Solano-Gallego & Masserdotti, 2023). The metastatic potential of TVT is low, although reported especially in immunosuppressed animals. When metastases occur, they commonly affect tissues and cavitory organs, such as the liver and spleen (Abeka, 2019).

The macroscopic characteristics of the lesion can vary greatly according to their anatomical location and it can manifest as solitary, multiple, nodular, or multilobulated, and can present variable dimensions. The surface of the tumor is commonly irregular, friable, ulcerated and displays a verrucous appearance. Cytopathological examination is a widely employed technique in TVT diagnosis because it is quick to perform, minimally invasive, and low-cost. Hence, this exam can indicate the correct clinical or surgical approach (Solano-Gallego & Masserdotti, 2023).

Frequent clinical signs in genital lesions involve serosanguinous or hemorrhagic secretions, frequent licking, pain, and discomfort, with the possibility of an ascending urinary tract infection (Ortiz, 2021). Depending on the size of the tumor mass, deformation and obstruction of the external genitalia may occur (Zupa et al., 2019).

As TVT is a neoplasm with low metastatic potential, this study aims to report a case of transmissible venereal tumor in a bitch, with splenic and thoracic metastatic foci.

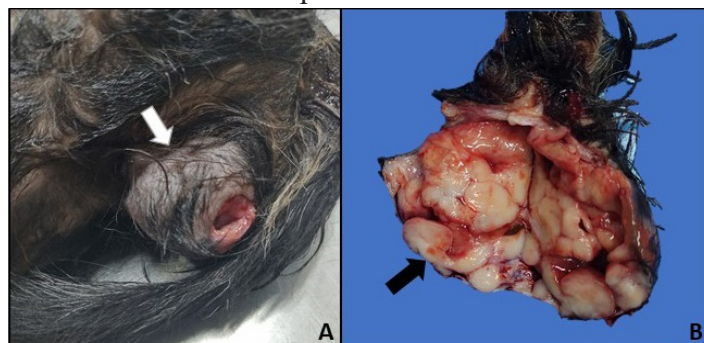
CASE REPORT

A female mixed breed canine cadaver of unknown age was sent to the Veterinary Pathology Laboratory of the Federal University of Parana (UFPR), Palotina Sector (Parana, Brazil). The patient was a stray lacking clinical history. Initially, the dog was referred to veterinary care by members of a local non-governmental organization due to a mass in the vulvar region. The increased mass volume was diagnosed as a transmissible venereal tumor (TVT) through fine-needle cytology. Furthermore, abdominal palpation detected an increased abdominal volume. Through ultrasound examination and chest X-ray, and due to the location of the mass, possible neoplastic or hemangiosarcoma foci were noticed. Due to the animal's clinical picture suggesting cavitory neoplasms, in addition to the absence of a caretaker, the patient was euthanized. To further elucidate the case, a necroscopic examination was

performed with subsequent collection of histopathological material for examination.

Macroscopic evaluation verified that the female dog was light weighted (body score 2/5), and that there was an irregular, rounded, soft and friable structure in the vagina and vulva (Figure 1A). Measuring approximately 4.5 cm x 4.2 cm x 3.2 cm, when cut, it was whitish, smooth and with homogeneous appearance when cut (Figure 1B). Observation of the abdominal cavity confirmed that the animal was not neutered. Furthermore, an irregular, soft, friable, and whitish mass was noticed in the spleen's caudal pole (Figure 2A), measuring 10.0 cm x 15.0 cm x 8.0 cm, as was another regular structure presenting the same characteristics described above, measuring 5.5 cm x 3.0 cm x 2.1 cm in the cranial pole (Figure 2A). When cut, both structures were very similar, with a soft, homogeneous, and whitish appearance (Figure 2B).

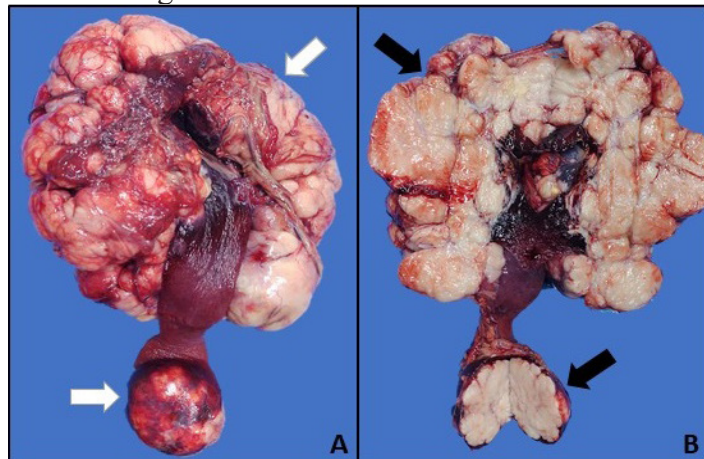
Figure 1
Genital TVT macroscopical lesion.



Source: Laboratory of Veterinary Pathology (Laboratório de Patologia Veterinária - UFPR).

Note. A: increased volume in the vulvar region (white arrow). B: sectioning shows the whitish and irregular appearance of the neoplasm (black arrow).

Figure 2
Macroscopic metastatic lesion of TVT in the spleen of a female dog.



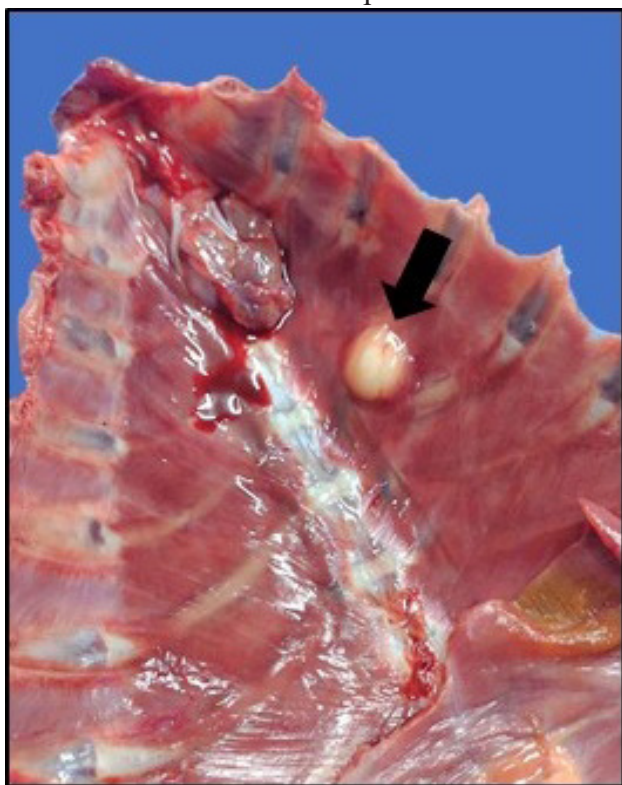
Source: Laboratory of Veterinary Pathology - UFPR.

Note. A: two neoplasms in the cranial and caudal poles of the parietal surface of the spleen (white arrow). B: whitish and homogeneous aspect of the sectioned neoplasms (black arrows).

In the parietal pleural cavity, between the fourth and fifth intercostal spaces, a structure with the previously described characteristics was observed, adhered to the musculature, measuring approximately 1.2 cm x 1.0 cm x 0.5 cm (Figure 3). The lungs were diffused and moderately reddish. Multifocal to coalescent and slightly whitish areas (emphysema) were observed at the edges of the lobes, on the left side.

Figure 3

TVT in a dog. Presence of whitish nodular neoplasm in the parietal pleura, between the fourth and fifth intercostal spaces.



Source: Laboratory of Veterinary Pathology – UFPR.

For cytological material collection, fine-needle aspiration (FNA) and indirect imprint techniques were chosen. For the FNA, the collected material was placed on a glass slide and another overlaid slide was used to gently compress and slide the material (squash preparation method). Romanowsky staining (panoptic) was used on the slides under light microscopy for evaluation.

The cytological evaluation revealed a similar morphological pattern in all three tissues, with high cellularity composed of round single-layered cells with a high nucleus to cytoplasm ratio. The cytoplasm was scant, slightly bluish, and multiple coarse vacuoles were present. The nuclei were eccentric, with dense chromatin, and some large and prominent nucleoli. Moderate anisocytosis and anisokaryosis with rare mitotic figures were also present. The cellular features observed in the cytological evaluation were consistent with the lymphocytic differentiation of TVT (Figure 4A).

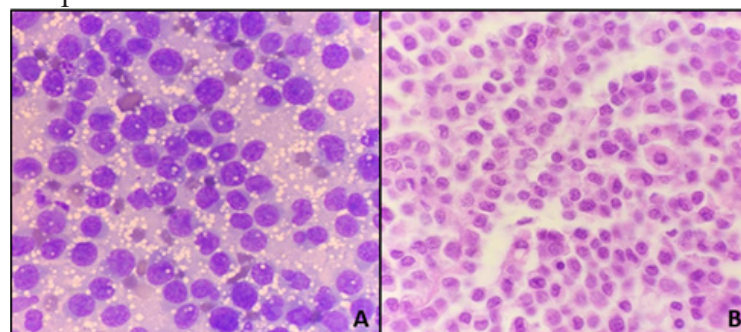
The collected fragments were fixed in 10% formaldehyde and subsequently processed following

the guidelines described by Tolosa, Rodrigues, Behmer e Freitas (2003). The cellular alterations found in the vulva, spleen, and parietal pleura exhibited similar morphological patterns in the histopathological evaluation. The researchers observed a densely cellular neoplastic proliferation of non-infiltrative encapsulated round cells. The cells were large with indistinct borders, arranged in clustered mantles, separated by moderate fibrovascular stroma.

The cytoplasm was eosinophilic, ranging from scant to moderate, and some cells exhibited mild vacuolization. The nuclei were rounded, large, and paracentral with loose chromatin, and some showed a single nucleolus. Anisocytosis and anisokaryosis were moderate (Figure 4B). A discreet inflammatory infiltrate composed of plasma cells, lymphocytes, and foamy macrophages was interspersed with the neoplastic cells.

Figure 4

Photomicrograph of cytological and histopathological samples of TVT.



Source: Laboratory of Veterinary Pathology – UFPR.

Note. A: cytological evaluation from the spleen showing the presence of round cells with scanty and vacuolized cytoplasm, panoptic stain, 40x. B: histological evaluation from the thoracic cavity showing neoplastic proliferation of round cells with slightly eosinophilic cytoplasm and rounded nuclei, hematoxylin-eosin stain (HE), 40x.

DISCUSSION

Extragenital TVT located in the spleen and chest cavity is uncommon and poorly documented, as this type of metastasis is considered rare. The extragenital manifestation of this tumor can occur in two ways. The first is a consequence of natural implantation in sites of wounds and bites, especially in patients without external genital lesions (Withrow, Vail & Page, 2012). The second is through metastasis, when there is primary involvement of genital organs (Amaral, Gaspar, Silva & Rocha, 2004; Batista et al., 2007), as observed in the present study.

Young, immunosuppressed animals and male dogs present a higher chance of developing metastases (Ganguly, Das & Das, 2016). Moreover, stray and non-neutered dogs are also more predisposed to develop this neoplasm (Costa & Castro, 2016). Due to the scarcity of clinical history and lack of complementary tests, little can be inferred about the age and immunosuppressive diseases of the patient. However, the evaluated animal had a compromised body condition (score 2/5), which may have contributed to the immunosuppression development.

The cytopathological diagnosis of TVT is extremely important, as it allows classifying the disease based on cellular morphology, distinguishing between plasmacytic, lymphocytic, and mixed TVT subtypes. When there is a predominance of cells exhibiting a high nucleus to cytoplasm ratio, which resemble a lymphocyte, the TVT is classified as lymphocytic. When the cells have a plasmacytic appearance, an oval and eccentric nucleus, and a low nucleus to cytoplasm ratio, the TVT is called plasmacytic. In turn, mixed classification occurs when the observed cellularity contains a similar proportion of plasmacytic and lymphocytic cells (Mukaratirwa & Gruys, 2003; Amaral, 2005).

The morphological variation of TVT is responsible for changes in the biological behavior of the tumor (Valençuela et al., 2015). Studies show that the plasma cell subtype has greater aggressiveness, malignancy, metastatic potential, and resistance to chemotherapeutic therapies. Thus, the treatment is longer and the prognosis less favorable, besides having a higher incidence when compared to other classifications (Paranzini, Sant'anna, Santis & Martins, 2015). These factors highlight the importance of using cytological examination for subtype classification. In the present case, cells with a high nucleus to cytoplasm ratio were evident, which classifies the TVT as lymphocytic.

The histological appearance of TVT consists of proliferating round to oval-shaped cells, arranged in uniform cell sheets and sometimes in clusters. The morphological characteristics consist of round or oval-shaped, centralized nuclei; single prominent nucleoli; slightly basophilic, homogeneous cytoplasm; and the presence of fine granulations and vacuoles. The microscopic features are very similar to other round cell neoplasms, especially mastocytomas and lymphomas; therefore, immunohistochemical evaluation is necessary (Agnew & MacLachlan, 2017). However, in the present case, the association of clinical, cytological, necroscopic, and histopathological findings, including macroscopic and microscopic evaluation of the lesions, was sufficient for the diagnosis of metastatic TVT.

It is important to perform differential diagnosis of other round cell neoplasms in dogs, such as mastocytoma, lymphoma, plasmacytoma, and non-neoplastic granulomatous lesions, as well as to distinguish between the three subtypes of morphological presentations of TVT, which often present distinct biological behavior (Amaral, 2005).

In the present case, the clinical and macroscopic

aspects of the lesions located in the external genitalia allowed adding TVT as a differential diagnosis. The severe splenic involvement observed on ultrasound examination led to the clinical suspicion of lymphoma or metastatic hemangiosarcoma, which are neoplasms of poor to unfavorable prognosis, culminating in the euthanizing of the animal. TVT metastases tend to occur mainly in lymph nodes, but their presence in the central nervous system, mammary gland, and abdominal, and thoracic cavity organs, such as lungs, spleen, uterus, and ovaries, have been reported (Pereira, Silva, Martins, Ferreira & Brooks, 2000; Bastan, Acar & Cengiz, 2008; Santos et al., 2012; Fonseca et al., 2014; Hendrick, 2017; Solano-Gallego & Masserdotti, 2023). Also, its occurrence should not be excluded in patients with TVT genital masses.

There are several therapeutic resources for the treatment of TVT, the most common being chemotherapy because it is an efficient treatment and shows results in most cases. Other methods, such as surgery and radiation therapy, are rarely used due to high chance of recurrence and high-cost.

The standard chemotherapy protocol recommended in literature is weekly intravenous vincristine sulfate, with four to eight applications for complete remission. In cases of drug-refractory TVT, another alternative is doxorubicin, applied intravenously every 21 days. Spontaneous regression is reported in cases of experimental TVT, however, which is not common in natural pictures of the disease and requires therapeutic intervention (Costa & Castro, 2016). Although chemotherapy is extremely efficient in the treatment of this neoplasm, the correct diagnosis of the neoplasm became unfeasible in this case due to the difficulty and cost of diagnosing cavity masses, and the animal was referred for euthanasia.

CONCLUSION

Based on the pathological findings, the diagnosis of transmissible venereal tumor (TVT) with distant metastases involving the spleen and pleura can be confirmed. In addition, it is emphasized that TVT should be included in the list of differential diagnoses of intracavitary neoplasms, especially involving large splenic masses.

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REFERENCES

- Abeka, Y. T. (2019). Review on canine transmissible venereal tumor (CTVT). *Cancer Therapy & Oncology International Journal*, 14(4), pp. 1–9. doi: 10.19080/CTOIJ.2019.14.555895
- Agnew, D. W., & MacLachlan, N. J. (2017). Tumors of the genital systems. In Meuten, D. J. (Ed.), *Tumors in domestic animals* (5ed., pp. 689–722). New Jersey, EUA: John Wiley & Sons Inc.

- Amaral, A. S. (2005). *Tumor venéreo transmissível canino: critérios citológicos de malignidade e caracterização citomorfológica correlacionada a imunocitoquímica e lesões de DNA* [Tese de doutorado em Medicina Veterinária, Universidade Estadual Paulista]. UNESP. <http://hdl.handle.net/11449/101297>
- Amaral, A. S., Gaspar, L. F. J., Silva, S. B., & Rocha, N. S. (2004). Exame citológico como método diagnóstico do tumor venéreo transmissível na região de Botucatu, Brasil (Estudo Retrospectivo: 1994-2002). *Revista Portuguesa de Ciências Veterinárias*, 99(551), pp. 167-171.
- Bastan, A., Acar, D. B., & Cengiz, M. (2008). Uterine and ovarian metastasis of transmissible venereal tumor in a bitch. *Turkish Journal of Veterinary & Animal Sciences*, 32(1), pp. 65-66.
- Batista, J. S., Soares, H. S., Pereira, R. H. D. M. A., Petri, A. A., Sousa, F. D. N., & Nunes, F. D. C. R. (2007). Tumor venéreo transmissível canino com localização intraocular e metástase no baço. *Acta Veterinária Brasilica*, 1(1), pp.45-48. doi: 10.21708/avb.2007.1.1.259
- Costa, M. T., & Castro, K. F. (2016). Tumor venéreo transmissível canino. In Daleck, C. B., & Nardi, A. B (Ed.). *Oncologia em cães e gatos*. (2ed, pp. 990-1008). Rio de Janeiro, RJ: ROCA.
- Daleck, C. R., & Nardi, A. B. (2016). *Oncologia em cães e gatos*. Rio de Janeiro, RJ: ROCA.
- Fonseca, L. S., Silva, S. M. M. S., Rocha, H. J., Neto, Horta, R. S., Quessada, A. M., & Miranda, D. F. H. (2014). Tumor venéreo transmissível (TVT) com metástase para a glândula mamária. *Acta Scientiae Veterinariae*, 42(Suppl 1), pp. 1-6.
- Ganguly, B., Das, U., & Das, A. K. (2016). Canine transmissible venereal tumour: a review. *Veterinary and Comparative Oncology*, 14(1), pp. 1-12. doi: 10.1111/vco.12060
- Hendrick, M. J. (2017). Mesenchymal tumors of the skin and soft tissues. In Meuten, D. J. (Ed.), *Tumors in domestic animals* (5ed. pp. 142-175). New Jersey, EUA: John Wiley & Sons Inc.
- Mukaratirwa, S., & Gruys, E. (2003). Canine transmissible venereal tumour: cytogenetic origin, immunophenotype, and immunobiology. A review. *Veterinary Quarterly*, 25(3), pp. 101-111. doi: 10.1080/01652176.2003.9695151
- Ortiz, L. S. (2021). *Tumor venéreo transmissível (TVT) canino: epidemiologia, diagnóstico e terapêutica* [Trabalho de Conclusão de Curso de Medicina Veterinária, Centro Universitário do Sul de Minas]. UNIS. <http://repositorio.unis.edu.br/handle/prefix/1849>
- Paranzini, C. S., Sant'anna, M. C., Santis, G. W., & Martins, M. I. M. (2015). Prevalence of different cytomorphological types of transmissible venereal tumours and the association with prognosis in dogs treated with vincristine sulphate: retrospective study. *Semina: Ciências Agrárias*, 36(6), pp.3795-3800.
- Pereira, J. S., Silva, A. B. F., Martins, A. L. B., Ferreira, A. M. R., & Brooks, D. E. (2000). Immunohistochemical characterization of intraocular metastasis of a canine transmissible venereal tumor. *Veterinary Ophthalmology*, 3(1), pp.43-47. doi: 10.1046/j.1463-5224.2000.00097.x
- Pimentel, P. A. B., Oliveira, C. S. F., & Horta, R. S. (2021). Epidemiological study of canine transmissible venereal tumor (CTVT) in Brazil, 2000-2020. *Preventive Veterinary Medicine*, 197, p. 105526. doi: 110.1016/j.prevetmed.2021.105526
- Santos, C. R. D. S., Ruschi, C. S., Elias, T., Cruz, C. F. G. D., Bonamin, J. G. X., & Villano, L. (2012). Metástase visceral de tumor venéreo transmissível em cão. *Veterinária e Zootecnia*, 16(3), pp. 465-470.
- Solano-Gallego, L., & Masserdotti, C. (2023). Reproductive system. In Raskin, R. E., Meyer, D. J., & Boes, K. M. (Eds.). *Canine and feline cytopathology: a color atlas and interpretation guide* (4ed., pp. 1934-1939). Rio de Janeiro, RJ: ELSEVIER.
- Tolosa, E. M. C., Rodrigues, C. J., Behmer, O. A., & Freitas, A. G., Neto. (2003) *Manual de técnicas para histologia: normal e patológica*. Barueri, SP: Manole.
- Valençoa, R. A., Antunes, T. R., Sorgatto, S., Oliveira, B. B., Godoy, K. C. S., & Souza, A. I. (2015). Aspectos citomorfológicos e frequência dos subtipos de tumor venéreo transmissível canino no município de campo grande, MS, Brasil. *Acta Veterinaria Brasilica*, 9(1), pp. 82-86. doi: 10.21708/avb.2015.9.1.5261
- Withrow, S. J., Vail, D. M., & Page, R. L. (2012). *Small animal clinical oncology*. Amsterdam, Holanda: Elsevier Health Sciences.
- Zupa, A. E., Oliveira, A. A., Theodoro, W., & Lúcio, C. F. (2019). Tumor venéreo transmissível em cães: revisão de literatura. *Revista Saúde-UNG-Ser*, 13(2 Esp), pp. 109-110.