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REVIEW

Transmissible Venereal Tumor: A Review

Mehmet UÇAR

Afyon Kocatepe University, Faculty of Veterinary Medicine, Obstetrics and Gynecology Department, Afyonkarahisar/TURKEY

Corresponding author e-mail: mucar@aku.edu.tr

ABSTRACT

Transmissible venereal tumor (TVT) is a neoplasm that can be transmitted between female and male dogs via mating by the physical transfer of viable tumor cells. The tumor may spread to different parts of the body through sniffing, licking, scratching or biting affected lesions. It can be also observed in wild carnivores. TVT is mostly located in the posterior wall of the vagina, in the joint of vaginal vestibule and vagina in female dogs, while it is usually located in caudal part of the penis in males. Initially, the tumor is small and varying from pink to red, subsequently progressing to a large, ulcerated, and contaminated mass. By the time, the tumor's volume increases and the lesions become friable, hyperemic, hemorrhagic, multilobular and cauliflower-like masses. A serosanguinous vaginal discharge is observed. Definitive diagnosis is based on anamnesis, location of the mass, cytological and histological findings. The cells in the slides vary from round to oval or variable shapes and contain a pale blue or colorless cytoplasm with a single distinctive nucleus. They include small, light, clear intracytoplasmic vacuoles. TVT should be immediately treated as soon as diagnosed because there is no method to prevent it. Chemotherapy is the effective method for the treatment of TVT with the intravenous use of vincristine sulfate, which is a chemotherapeutic agent, once in a week for approximately three weeks applications. The cure rate varies at 90-95%. In this review, the incidence, etiopathogenesis, clinical findings, diagnosis, prognosis and therapies of TVT have been emphasized.

Key Words: Diagnosis, Etiopathogenesis, Incidence, Prognosis, Transmissible Venereal Tumor, Treatment

Transmisibil Venereal Tümör: Derleme

ÖZ

Transmisibil Venereal Tümör (TVT), erkek ve dişi köpeklerin çiftleşme sırasında canlı tümör hücrelerinin fiziksel transferi ile bulaşabilen neoplastik bir yapıdır. Tümör etkilenen lezyonların koklanması, yalanması, tırmalanması ve ısırılmasıyla vücudun farklı bölgelerine yayılabilir. TVT aynı zamanda vahşi kornivorlarda da gözlenebilir. Tümör genellikle erkek köpeklerde penisin kaudal kısmında lokalize olurken, dişilerde çoğunlukla vajinanın posteriyör bölgesinde, vestibulum ve vajinanın birleşme yerinde şekillenir. İlk başlarda tümör küçük ve pembeden kırmızı renge değişen şekildedir, daha sonra büyük ülserasyonlu ve kontamine bir kitle haline dönüşür. İlerleyen zamanlarda tümörün hacmi artar ve şekillenen lezyonlar multilobüler, karnıbahar görünümünde olup gevrek, hiperemik ve hemorajik yapıdadırlar. Serösangionöz vajinal akıntı gözlenir. Tümörün kesin tanısı anemnez bilgilerine, kitlenin oluşum yerine, sitolojik ve histolojik bulgulara dayanmaktadır. Preparatlardaki hücreler yuvarlak, oval veya değişik yüzeyli yapıda olup, solgun mavi veya renksiz sitoplazma ile belirgin bir nükleus içerirler. Hücrelerde küçük, parlak ve temiz görünümlü intrastoplazmik vakuoller bulunur. TVT'nin oluşumunu tamamen engelleyecek bir yöntem olmadığı için, teşhis edildiğinde derhal tedavi edilmesi gerekir. Kemoterapi TVT için etkili bir sağaltım yöntemidir. Kemoteröpatik ajan olan vinkristin sülfatın haftada bir kez, ortalama 3 hafta süreyle damar içi yolla verilmesi sonrasında iyi sonuçlar alınmaktadır. Tedavi oranı %90-95 arasındadır. Sunulan bu derlemede, TVT'nin insidansı, patogenezi, klinik bulguları, tanısı, prognozu ve tedavisi üzerinde durulmuştur.

Anahtar Kelimeler: Diagnoz, Etiyopatogenez, Incidens, Prognoz, Tedavi, Transmisibil Venereal Tümor

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INTRODUCTION

Tumors are the most common of mortal disorders observed in humans and animals. Among mammals, they are observed most frequently in dogs. Transmissible venereal tumor (TVT) is one of the most uncontrolled spreading tumor via mating that disrupt the comfort of life of dogs.

TVT, which is the most common of genital tract tumors of canine species, is also known as canine Sticker's sarcoma, venereal granuloma, contagiosum venereal sarcoma, contagiosum lymphosarcoma, canine condyloma, contagiosum lymphoma and infectious sarcoma (Rogers 1997, Smith and Washbourn 1998, Gurel et al. 2002). It has a relatively high incidence rate among all tumor types (Tella et al. 2004). In this review, the most critical points of TVT are emphasized.

Incidence

In many countries of the world TVT is observed in both sexes (Smith and Washbourn 1998, Strakova and Murchison 2014) except Antarctica (Das and Das 2000). Female dogs are contaminated with TVT more than males because only one infected male often mates with numerous females. TVT is rare in home-kept dogs (Ganguly et al. 2016). Although the low frequency of the tumor depends on the development level of the countries (Strakova and Murchison 2014). It is commonly observed in young and sexually active stray dogs in urban areas where mating is not under control (Hayes et al. 1983, Rogers 1997, Das and Das 2000, Gurel et al. 2002). It is mostly seen in tropical and subtropical climates (Hayes et al. 1983, Rogers 1997), it may also be observed in all geographical conditions (Hayes et al. 1983). It has been primarily reported in India and incidence rates vary between 23 and 43% (Chaudhary and Rao 1982, Gandotra et al. 1993, Jain et al. 2002).

The occurrence and duration incidence rate of the tumors also depend on the condition of immune system of the animal. It has been reported that it progresses benignly and can regress in those animals with good general body condition (Higgins 1966, Yang and Jones 1973, Vermooten 1987), while the development of the tumor is severe and tends to metastasize in too young or too old animals with suppressed immune systems (Higgins 1966, Yang and Jones 1973).

Etiopathogenesis

TVT is the first tumor type that the transmission occurs from animal to animal during mating (Rogers 1997). Although it is often observed in the external genitalia of female stray dogs (Smith and Washbourn 1998), it can also be developed in the internal genitalia (Rogers 1997, Gurel et al. 2002, Purohit 2009). The extra-genital tumors may be observed in higher rates due to the sexual behavior of the males (Hamir 1985, Pandey et al. 1989). Transmission of TVT occurs more easily if there is a clear damage on the surface of genital mucosal layer. During the mating, when the female is in standing heat, tissue damages form in the genital tract of the female owing to the enlargement of the infected penis and prolonged mating time. Subsequently the separation of the dogs after mating allows TVT to spread (Murchison 2009). Moreover, the behaviors of the dogs like sniffing, licking, scratching or biting can spread the tumor to different parts of the body (Rogers 1997, Das and Das 2000, Gurel et al. 2002). It is considered that the neoplastic cells which are peeled off by the physical contact during licking, sniffing, scratching or biting are transferred to opposite genital tract, nasal and oral mucosa, rectum or skin (Albanese et al. 2002, Amaral et al. 2007, Rezaei et al 2016). Therefore, in primal TVT cases, it is possible to see the detectable lesions in the skin, face, nasal or oral cavity, eyes and subcutaneous tissues together with the external genitalia (Rogers 1997, Das and Das 2000, Brandao et al. 2002, Gurel et al. 2002, Rezaei et al 2016). It can be also observed in wild carnivores such as wolf, coyote and fox (Rogers 1997, Das and Das 2000, Gurel et al.2002).

Several hypotheses have been proposed for the pathogenesis of transmission of TVT. It has been reported that the transmission may be associated with a viral agent (Cockrill and Beasly 1975) or it is not related to any virus, since oncogenic viral particles haven't been detected in the tumor cells by electron microscopy (Moulton 1990). Concerning the view of cytological and immunological studies, the most possible way for spreading of TVT is direct cell transplantation (Higgins 1966, Richardson 1981, Mozos et al. 1996, Mukaratirwa and Gruys 2003). The neoplastic cell is almost a stranger for the tissue. During mating, the tumor cells passing the barrier of major histocompatibility complex (MHC) among the same species or even other species of canine family such as fox and coyote and protecting its viability and vitality can be transplanted as an allograft to other animal's genital tract (Higgins 1966, Mukaratirwa and Gruys 2003, Murgia et al. 2006). Oncologically, TVT is the first and unique tumor type which has been proven that the viable tumor cells experimentally can be transferred from one animal to another (Das and Das 2000). Therefore, TVT are also known as allogeneic cell transplants (Richardson 1981, Mozos et al. 1996). In addition, it has been stated that the transplantation of viable TVT cells can be performed in healthy animals carrying only the same MHC antigens (Murgia et al. 2006).

It has been reported experimentally that transfer of TVT is progressed in three different stages. These are progressive, stabile and regression phases (Chu et al. 2001, Liao et al. 2003). The duration of progressive phase takes a couple of weeks and the tumor becomes palpable in 10-20 days following the experimental transfer (Chu et al. 2001). It is expressed that there is a slow but palpable growth period for 20 days in stabile phase of the tumor (Mukaratirwa et al. 2006), then it just passes to the regression phase and the tumor shrinks or disappears in the period of several weeks or months (Chu et al. 2001, Liao et al. 2003). Interestingly, some tumors (1-20%) grow rapidly following a second development phase and cause metastasis without any regression phase (Chu et al. 2001). The spontaneous regression of the tumors is controlled by the immunity system (Liao et al. 2003). It is known that the infiltration of the defense system cells increases from the progressive phase to the regression (Mukaratirwa and Gruys 2003, Mukaratirwa et al. 2006, Stockmann et al. 2011). Spontaneous regression of both experimentally and naturally transplanted TVT is occurred by necrosis and apoptosis along with the infiltration of lymphocytes and plasma cells (Stockmann et al. 2011).

TVT is usually a benign tumor. However, cases developing slowly throughout several years transform into malignant form in nature and cause metastasis at a rate of 5-17% (Rogers 1997). Metastatic cases are more numerous in the male dogs (Hamir 1985, Pandey et al. 1989). The lymph nodes, skin and subcutaneous tissues, liver, spleen, kidneys, lungs, heart, skeletal muscle, central nervous system, thymus, glandula parotid, joints of metacarpal and the metatarsal bones, and udders are the reported metastatic areas (De Lorimier and Fan 2007). Besides these in a case report, metastases were observed even in the brain and eyes (Ferreira et al. 2000).

Clinical Aspect and Diagnosis

In male dogs, TVT is usually located in the caudal part of penis, from corpus to bulbus, or the glans penis, while it is rarely seen in prepuce (Das and Das 2000). In females, development of TVT mostly forms in the posterior wall of vagina, at the joint of vaginal vestibule and vagina (Stockmann et al. 2011). The lesions are small (in a diameter of 1-3 mm), superficial and varying from pink to red at the beginning of the tumor formation (Purohit 2009). In later times, the tumor's volume increases with a cauliflower-like nodular appearance. Although it is fragile, it has a red, hemorrhagic and hard structure. Nodular mass can reach up to 5-7 cm in diameter. The size of the mass can be 10-15 cm in diameter, if multilobulated subcutaneous lesions progress to deeper layers of mucosa. Moreover, it can be observed as pedunculated, nodular, papillary and multilobulated structures. The tumor can cover the external orificium of urethra and protrude from vulva labia (Purohit 2009). The tumor surface is often inflamed and may be infected (Brown et al. 1980). Leakage or simple bleeding as well as contamination or ulceration is visible in tumors (Ferreira et al. 2000, Das and Das 2000, Purohit 2009).

The clinical findings are less remarkable in male dogs. In these animals, bloody preputial discharge, redness, deformation and ulceration in preputial opening can be seen (Ferreira et al. 2000, Das and Das 2000). Due to complication of the case with infection, females may encounter difficulties in urination or dystocia due to mechanical obstruction. Phimosis and paraphimosis may be observed in males (Das and Das 2000, Birhan and Chanie 2015). Weakness, ulcers in the perineum, anorexia, constipation, mating refusal and weight loss are the less common observed symptoms (Ganguly et al. 2016). Contaminated animals are at a high risk of having bacteriuria by the tumor caused to urine retention (Batamuzi and Kristensen 1996). A long-lasting serosanguinous vaginal discharge is observed in the infected dogs. The anemia may be evident in case of intensive bleeding (Purohit 2009). The general health of animals is not reduced unless the lesions turn infected and necrotic or block the urethral orifice (Ganguly et al. 2016).

The diagnosis can be made depending on the anamnesis, location of the mass, unclean perineum, bloody discharge and typical appearance of the tumor, cytology and histology (Purohit 2009). Estrus bleeding, cystitis, urethritis and prostatitis should be taken into consideration for differential diagnosis (Das and Das 2000).

TVT has a typical cytologic appearance. The examination of smear preparations is recommended because the exfoliative cytology technique is affordable, simple, feasible, and minimally invasive. The shape of cells in the slides vary from round to oval or variable surface structures. The cells usually have a pale blue or colorless cytoplasm with a single distinctive nucleus. Also they contain small, light, clear intracytoplasmic vacuoles and numerous mitotic figures (Hayes et al. 1983, Rogers 1997, Purohit 2009).

A definitive diagnosis requires the histopathologic examination of the biopsy sample. In histopathology, dense amount of round, oval or in variable shape tumor cells are usually located around blood or lymphatic vessels (Purohit 2009, Birhan and Chanie 2015). The size of the cell nucleus is higher than the cytoplasm. Cytoplasmic vacuoles are mostly visible. Lymphocytes, plasma cells and macrophages are

often observed (Birhan and Chanie 2015). The growing of tumor mass cause tightly integrated, irregular cell formation and fibroblasts are formed among them (Purohit 2009). Immunohistochemistry can be used for the diagnosis of metastatic tumors following combination of clinical findings (Birhan and Chanie 2015).

Treatment and Prognosis

In the treatment of TVT, various options such as surgery, radiotherapy, immunotherapy, biotherapy or chemotherapy are used (Purohit 2009). Although surgery can be effective for small and localized tumors, recurrence rate following the surgery can reach up to 30-75% in metastatic cases (De Lorimier and Fan 2007). During surgery, the operation site can be contaminated with TVT cells and the risk of reoccurrence may increase (De Lorimier and Fan 2007, Purohit 2009). Therefore, surgery is not a preferred treatment method for TVT. However, cauterization, electrosurgery or cryosurgery may prevent the recurrence of TVT, subsequent to surgery (Idowu 1985, Rao et al. 1993, Hoque 1995).

TVT is a radiosensitive tumor and substances generating orthovoltage (Thrall 1982) or megavoltage (Rogers et al. 1998) like cobalt are used for this purpose. Radiotherapy, as an alternative to chemotherapy treatment in TVT, can be used for the treatment-resistant lesions or the lesions forming in brain, testis or eyes. However, the difficulties in application, lack of adequate equipment and the need for longer application period than the chemotherapy, are the main disadvantages of the method (De Lorimier and Fan 2007).

Biotherapy is limited for the treatment of TVT. Intratumor Calmette-Guérin's bacillus (BCG) administration for three weeks has a little success (Johnston 1991) and high reoccurrence rates have been reported subsequent to the treatment (Richardson 1981, Vermooten 1987). Moreover, the vaccines obtained from Staphylococcus protein A, BCG or the tumor cells for immunotherapy have also recurrence risks (Rogers 1997, Mukaratirwa and Gruys 2003).

Chemotherapy is the most common and effective method for the treatment of TVT (Amber et al. 1990). Favorable results have been derived from the intravenous (IV) use of vincristine sulfate, which is a chemotherapeutic agent, at doses of 0.5-0.7 mg/m2 of body surface area or 0.025 mg/kg once in a week for approximately three consecutive weeks (Amber et al. 1990, De Lorimier and Fan 2007). Before the initialization of vincristine sulfate chemotherapy, assessment of general health status of the animal is essential. During therapy, at weekly intervals, it is essential to analyze the total number of leukocytes (Ganguly et al. 2016). It is necessary to dilute vincristine sulfate with saline and to administer this combination as a very slow IV infusion by protecting it from direct sunlight. The treatment must be continued until no observable symptoms of the tumor remains and average administration duration is about 2-6 weeks. The overall cure rate varies between 90-95% (De Lorimier and Fan 2007). A transient deterioration of semen quality can be observed that quickly returns to normal within 15 days following the final application in male dogs treated with vincristine sulfate (Saratsis et al. 2000, Gobello and Corrada 2002).

Subsequent to chemotherapy, a distinctive regression in neoplastic formation usually begins two weeks after the first treatment. Even though no significant decreases were detected in AST and ALP enzymes, a significant decrease may be seen in the numbers of total serum protein, hemoglobin, total erythrocytes and total leukocytes thus neutropenia, eosinopenia, lymphocytosis, and monocytosis may be observed. Possible side effects include anorexia, vomiting, diarrhea, myelosuppression and alopecia. Unless a desirable result is obtained from vincristine sulfate, doxorubicin can be used IV at a dose of 1 mg/kg for a maximum of three weeks (Amber et al. 1990).

Another treatment approach to TVT is the combination of vincristine sulfate (0.0125mg/kg/per week, IV), methotrexate (0.3-0.5mg/kg/per week, IV) and cyclophosphamide (1mg/kg/per day, peros) can also be used until the visible symptoms disappear. The administration lasts about 4-6 weeks (Purohit 2009). Although Adriamycin (30 mg/m^2, IV, once in every three weeks) is also effective, it must be used only in the cases where vincristine sulfate is not effective, due to the side effects of Adriamycin (De Lorimier and Fan 2007).

In a study, it has been reported that a TVT case, which did not respond to successive treatments of vincristine sulfate, vinblastine and doxorubicin combination. Later the tumor was surgically removed and ovariohysterectomy performed on the very same day. Following this, the administration of L-asparaginase (400 IU/kg, SC) and oral prednisolone (during the first week 2 mg/kg, once in a day; the second week 1,5 mg/kg/day; the third week 1 mg/kg/day and the last week 0.5mg/kg/day) on the sixth day following the ovariohysterectomy have obtained successful results (Da Silva et al. 2014).

Good prognosis can be expected in most of the TVT cases following chemotherapy. However in such cases that are resistant to treatment, electrocauterization or cryocauterization were also reported to be useful choices of therapy (Vermooten 1987, Rogers 1997).

CONCLUSION

The contagious tumor of stray dogs, TVT, should be immediately treated as soon as diagnosed. It is obvious that there is no method to prevent it. However, two main precautions can help for prevention or spreading of the tumor. The main and first approach is to inform the owners about the importance of ovariohysterectomy, in cases no further breeding is required by the owner. Secondly, to inform the owners about the importance of gynecological examinations performed at least two times per year, if the owners do not prefer to demand elective ovariohysterectomy.

REFERENCES

Albanese F, Poli A, Millanta F, Abramo F. Primary cutaneous extragenital canine transmissible venereal tumour with Leishmania laden neoplastic cells: a further suggestion of histiocytic origin. Vet Dermatol. 2002;13: 243-246.

Amaral AS, Sandra BS, Isabelle F, Fonseca LS, Andrade FH, Gaspar LF, Rocha NS. Cytomorphological characterization of transmissible canine venereal tumor. Rev Port Cienc Vet. 2007;102: 253-260.

Amber EL, Henderson RA, Adeyanju JB, Gyand EO. Single drug chemotherapy of canine transmissible venereal tumour with cyclophosphamide methotrexate or vincristine. J Vet Int Med. 1990; 4:144-147.

Batamuzi EK, Kristensen F. Urinary tract infection: the role of canine transmissible venereal tumour. J Small Anim Pract. 1996;37: 276-279.

Birhan G, Chanie M. A Review on Canine Transmissible Venereal Tumor: from Morphologic to Biochemical and Molecular Diagnosis. Acad J Anim Diseases. 2015;4(3): 185-195.

Brandao CV, Borges AG, Ranzani JJT, Rahal SC, Teixeira CR, Rocha NS. Transmissible venereal tumour in dogs: a retrospective study of 127 cases (1998-2000). Rev Educ Contin CRMV SP. 2002;5:25-31.

Brown NO, Calvert C, Mac Ewen EG. Chemotherapeutic management of transmissible venereal tumour in 30 dogs. J Am Vet Med Assoc. 1980;176: 983–986.

Chaudhary C, Rao MRK. Certain canine neoplasms encountered in Andhra Pradesh. IndianVet J. 1982;59: 100-102.

Chu RM, Lin CY, Liu CC, Yang SY, Siao YW, Hun SW. Proliferation characteristics of canine transmissible venereal tumor. Anticancer Res. 2001;21: 4017-4024.

Cockrill JN, Beasly JN. Ultrastructural characteristics of canine transmissible venereal tumor various stages of growth and regression. Am J Vet Res. 1975;36(5): 677-681.

Da Silva DM, Reusing MSO, Franciosi AI, Belo CEP, Goncalves KA, De Souza RS, Guerios SD. Treatment of canine transmissible venereal tumor using L-asparaginase, prednisone, and surgery in a clinical chemotherapy-resistant case. Turk J Vet Anim Sci. 2014; 38: 220-223.

Das U, Das AK. Review of canine transmissible venereal sarcoma. Vet Res Comm. 2000; 24:545-556.

De Lorimier LP, Fan TM. Canine Transmissible Venereal Tumor. In: Withrow SJ, Vail DM eds. Withrow & MacEwen's Small animal clinical oncology. 4 th ed. USA:Saunders Elsevier, 2007; pp.799-804.

Ferreira AJA, Jaggy A, Varejaop AP, Ferreira MLP, Correia JMJ, Mulass JM, Almeida O, Oliveira P, Prada J. Brain and ocular metastases from a transmissible venereal tumour in a dog. J Small Anim Pract. 2000;41: 165-168.

Gandotra VK, Chauhan FS, Sharma RD. Occurrence of canine transmissible venereal tumor and evaluation of two treatments. Indian Vet J. 1993;70: 854-857.

Ganguly B, Das U, Das AK. Canine transmissible venereal tumour: a review. Vet and Comp Oncol. 2016;14:(1) 1-12

Gobello C, Corrada Y. Effects of vincristine treatment on semen quality in a dog with a transmissible venereal tumour. J Small Anim Pract. 2002;43: 416–417.

Gurel A, Kuscu B, Gulanber EG, Arun SS. Transmissible venereal tumors detected in the extragenital organs of dogs. Israel J Vet Med. 2002;57:23-26.

Hamir AN. Primary penile and nasal transmissible venereal tumour in a dog. Australian Vet J. 1985; 62: 430-432.

Hayes HM, Biggar RJ, Pickle LW, Hoover R, Toft JD**.** Canine transmissible venereal tumor:

a model for Kaposi's sarcoma? Am J Epidemiol. 1983; 117:108-109.

Higgins DA. Observations on the canine transmissible venereal tumor as seen in the Bahamas. Vet Rec. 1966;79(3): 67-71.

Hoque M. Different modes of therapy for canine transmissible venereal tumor. Veterinarian. 1995;19:1-2.

Idowu AL. Cryosurgery of canine transmissible venereal tumor. Tropical Vet. 1985;3:74-78.

Jain A, Tiwari RP, Tiwari SK, Awasthi MK. Clinical observations in TVT effected dogs treated with vincristine sulfate. Indian J Anim Reprod. 2002;23 (1):71-72.

Johnston SD. Performing a complete canine semen evaluation in a small animal hospital. Vet Clin N Am Small Anim Pract. 1991; 21(3):545-551.

Liao K, Hung S, Hsiao Y, Bennett M, Chu RM. Canine transmissible venereal tumor cell depletion of B lymphocytes: molecule(s) specifically toxic for B cells. Vet Immunol Immunopathol. 2003;92: 149-62.

Moulton JE. Tumors of domestic animals. 3rd ed. University of California Press Berkley and Los Angeles. 1990;10: 498-502.

Mozos E, Mendez A, Gomez-Villamandos JC, Martin De Las Mulas J, Perez J. Immunohistochemical characterization of canine transmissible venereal tumor. Vet Pathol. 1996;33: 257-263.

Mukaratirwa S, Gruys E. Canine transmissible venereal tumor: cytogenetic origin, Immunophenotype and immunobiology. A review. Vet Q. 2003;25(3):101-111.

Mukaratirwa S, Chiwome T, Chitanga S, Bhebhe E. Canine transmissible venereal tumour: assessment of mast cell numbers as indicators of the growth phase. Vet Res Commun. 2006;30: 613-621.

Murchison EP. Clonally Transmissible Cancers in Dogs and Tasmanian Devils. Oncogene. 2009;27: 19-30.

Murgia C, Pritchard JK, Kim SY, Fassati A, Weiss RA. Clonal origin and evolution of a transmissible cancer. Cell. 2006;126: 477-487.

Pandey SK, Chandpuria VP, Bhargava MK and Tiwari SK. Incidence, treatment, approach and metastasis of canine transmissible venereal sarcoma. Indian J Anim Sci. 1989;59: 510–513.

Purohit G. Canine Transmissible Venereal Tumor: A Review. I J Vet Med. 2009;6(1): 1-6.

Rao TM, Kumar VG, Raghvender KBP, Joshi MR, Rao RLN. Cryosurgical treatment of transmissible venereal tumors. J Vet Anim Sci. 1993;24:149-152.

Rezaei M, Azizi S, Shahheidaripour S, Rostami S. Primary oral and nasal transmissible venereal tumor in a mix-breed dog. Asian Pac J Trop Biomed. 2016; 6(5):443-445.

Richardson RC. Canine transmissible venereal tumor. Comp Cont Educ Pract Vet. 1981;3:951-959.

Rogers KS, Walker MA, Dillon HB. Transmissible venereal tumor: a retrospective study of 29 cases, J Am Anim Hosp Assoc. 1998;34:463-470.

Rogers KS. Transmissible venereal tumor, Compend Contin Educ Pract Vet. 1997;19:1036-1045.

Saratsis P, Ypsilantis P, Tselkas K. Semen quality during vincristine treatment in dogs with transmissible venereal tumor. Theriogenology. 2000;53: 1185–1192.

Smith GB, Washbourn JB. Infective sarcomata in dogs. Br Med J. 1998;2: 1346-1347.

Stockmann D, Heitor FF, Alexandre LA, Rodrigo AL, Tereza CC, Maria CRL. Canine Transmissible Venereal Tumors: Aspects Related to Programmed Cell Death. Braz J Vet Pathol. 2011;4: 67-75.

Strakova A, Murchison EP. The changing global distribution and prevalence of canine transmissible venereal tumour. BMC Vet Research. 2014;10:168-.

Tella MA, Ajala OO, Taiwo VO. Complete regression of transmissible venereal tumor (TVT) in Nigerian mongrel dogs with vincristine sulfate chemotherapy. Afr J Bio Med Res. 2004;7(3):133-138.

Thrall DE. Orthovoltage radiotherapy of canine transmissible venereal tumors. Vet Radiol. 1982;23: 217-219.

Vermooten MI. Canine transmissible venereal tumour (TVT): a review. J S Afr Vet Assoc. 1987; 58: 147-150.

Yang TJ, Jones JB. Canine transmissible venereal sarcoma: transplantation studies in neonatal and adult dogs. J Natl Cancer Inst. 1973;51: 1915-1918.