Review article

Animal Reproduction Update

Year 2024, Volume-4, Issue-2 (July - December)

ACS Publisher
www.acspublisher.com

Therapeutics and Management of Persistent Cases of Canine Transmissible Venereal Tumour: An Update

Newton Biswas, Kiran Singh, Sushil Kumar, Sunil Parmar, Neeraj Srivastava*, M H Khan

Division of Animal Reproduction
ICAR-Indian Veterinary Research Institute, Bareilly-243122, Uttar Pradesh, India

ARTICLE INFO

Key Words: Diagnosis; lomustine; sticker's sarcoma; treatment; vincristine.

doi: 10.48165/aru.2023.4.2.1

ABSTRACT

The Canine Transmissible Venereal Tumour (CTVT) is a contagious venereal tumor in dogs. Mostly transmitted through sexual contact, it can also spread through sniffing, licking, biting, and scratching the affected area. It is a contagious tumour, mostly prevalent in mongrels and in dogs exhibiting high levels of sexual activity coupled with roaming behaviour in tropical and subtropical climates. Recently, the incidence of TVT has been found to be increasing, especially in urban areas, where pet parents often come across their animals showing oozing of serosanguinous fluid from anomalous tumorous growth in the external genitalia. This frequently turns out to be TVT. Cytological and histo-pathological findings are used to make a definitive diagnosis. Treatment options may include chemotherapy, surgery, radiotherapy, and immunotherapy, with chemotherapy often being the preferred choice. In recent times, pet owners have reported a recurrence of the case confirmed earlier as TVT. This has further implications for the development of toxicity due to the repeated use of chemotherapy. This necessitates an urgency to review the current therapeutic approaches and reformulate them with effective alternative regimens. Indeed, several new therapeutic protocols have been developed for TVT, which are very promising, especially for the cases that have shown resistance and recurrence to certain treatments. It is imperative that practicing veterinarians, besides being thorough about therapeutic knowledge, especially dosage calculation (body weight vs. body surface area), also get acquainted with preventive and control measures. This particular paper captures the manifold developments in different areas dealing with therapeutic alternatives, prevention, and control of TVT.

Introduction

Canine transmissible venereal tumour, also called transmissible venereal tumour (TVT), transmissible venereal sarcoma, venereal granuloma, infectious sarcoma, and Sticker's sarcoma, is a unique and intriguing form of cancer primarily affecting canines and has become a common challenge for many pet owners. It affects the external genitalia more frequently (Das and Das, 2000). Sometimes, it can also affect the skin and mucous membranes adjacent

*Corresponding author.
E-mail address: sangnee15@gmail.com (Neeraj Srivastava)
Received 22.05.2024; Accepted 03.06.2024

to the mouth, nose, and eyes. The clinical presentation of TVT, such as cauliflower-like ulceration, hemorrhagic, friable, irregular appearance, and bloody discharge, results in an awful situation for the owners (Setthawongsin et al., 2022). The owners then immediately seek veterinary attention and, eventually, treatment for the disease. The treatment includes radiotherapy, chemotherapy, immunotherapy, biotherapy, and excisional surgery (Ganguly et al., 2016). Nonetheless, the preferred treatment for TVT is chemotherapy. Vincristine sulphate is generally the most effective chemotherapeutic agent for TVT and the treatment of choice (Filho et al., 2020). But, due to incidences of recurrence and resistance to vincristine, recently, many agents and chemotherapy protocols such as cyclophosphamide, vinblastine, doxorubicin, and methotrexate have been gaining interest as alternatives to vincristine (Sewoyo and Kardena, 2022). It is also important to properly manage and control the spread of TVT. The contagious nature of this type of tumour may lead to the uncontrolled spread of the disease in a particular geographical region. A proper understanding of effective treatment regimens and a robust 'control and management' programme can only shake off the nuisance of TVT.

What is canine transmissible venereal tumour?

It is a contagious, transmissible, and benign type of cancer developed from skin histocytes and encountered in both sexes of any age and breed of dog. It predominantly affects adult sexually active dogs that roam. But the young ones and spayed bitches can also contract the disease (Alkan et al., 2017). One should note that TVT is not exclusively a venereal disease, as the cancerous growth may also spread through common social behaviours such as sniffing, licking, scratching, or biting (Purohit, 2009). Also, there are reports of dam-to-pup transmission through grooming and licking. It is important to understand CTVT from its origin and etiopathological point of view. It will help us gain more insights about its control, treatment, and management programs. Reports suggesting the viral origin of the diseases could not gain much ground as oncogenic viral particles remain undetected in affected cells (Çizmeci and Guler, 2018; Ayala-Díaz et al., 2019). Cytological and immunological studies have suggested the theory of direct cell transplantation, where the living cancer cell itself acts as infectious material. The viable cancer cells can easily pass the barrier of the major histocompatibility complex (MHC) and transplant themselves as allografts to the site of affection (Liao et al., 2003). TVT cells have an abnormal number of chromosomes, ranging from 57 to 64 (average 59) (Rebbeck et al., 2009). It is usually benign. It takes weeks to months to manifest its clinical form. It may also become malignant in certain cases (Bendas et al., 2022). The TVT cells can down regulate monocyte-derived dendrite cell differentiation (Liu et al., 2007). Dendrite cells are critical regulators of adaptive immune responses and are key cells in tumour antigen presentation (Gonzalez et al., 2000). By virtue of their secretion of tumour-derived immune-suppressive cytokines, TVT cells can limit the infiltration of inflammatory cells, namely T lymphocytes, plasma cells, and macrophages, into tumour tissue (Abeka, 2019). This leads to the abnormal proliferation of cancer cells without any biological regulation. Thus, in brief, some of the important attributes of TVT are that it is contagious, shows abnormal cytoarchitecture, is immunosuppressive, and is proliferative in nature; and control, treatment, and management regimens must be formulated by keeping these attributes of TVT in mind.

Clinical findings and diagnosis

TVT are typically found in the caudal part of the penis. In females, it forms on the posterior wall of the vagina. The lesions are small, superficial, and varying in colour. The tumour is red, hemorrhagic, and hard, with a nodular mass up to 5-7 cm in diameter. It can cover the urethra or protrude from the vulvar labia (Sankar et al., 2016). Male dogs show significant clinical findings, including bloody discharge, redness, and ulceration (Fig. 1). Females may experience difficulties with urination or dystocia due to complications arising from infected tumorous growth. Less common symptoms include weakness, ulcers, anorexia, constipation, mating refusal, and weight loss. Contaminated animals are at high risk for bacteriuria due to urine retention and long-lasting serosanguinous vaginal discharge.

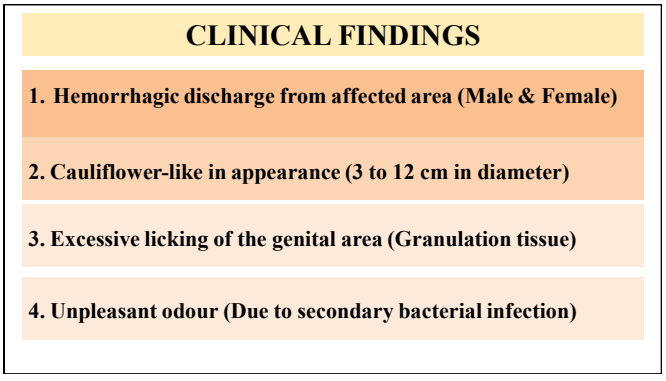

Fig 1: Most prominent clinical symptoms of Canine Transmissible Venereal Tumour (CTVT)

Diagnosis depends on anamnesis, bloody discharge, tumour appearance, cytology, and histology. Differential diagnosis should consider estrus bleeding, cystitis, urethritis, and prostatitis (Birhan and Chanie, 2015). Differential diagnoses of the TVT must include other round-cell

tumours such as histiocytomas, lymphoma, poorly differentiated mast cell tumours and carcinomas, and amelanotic melanomas. A cost-effective, simple, and minimally invasive exfoliative cytology technique using 'Giemsa staining' is recommended for quick diagnosis (Fig. 2). It involves examining cells in smear preparations with varying cell shapes and cytoplasm (Priyadarshini et al., 2021).

Histopathologic examination of biopsy samples is crucial for a definitive tumour diagnosis. Dense tumour cells are found around blood or lymphatic vessels, with a larger nucleus than cytoplasm (Jain et al., (2002). Lymphocytes, plasma cells, and macrophages are often observed. Immunohistochemistry can be used for metastatic tumour diagnosis (Fig. 3; Küçükbekir et al., 2021).

Differential diagnoses

Differential diagnoses comprise amelanotic melanomas, poorly differentiated mast cell tumours, lymphomas, histiocytomas, and carcinomas, among other round-cell tumours. Differentiating transmissible venereal tumours from other neoplasms such as hemangiosarcoma is crucial for all canine preputial tumours, as there are significant variations in treatment and prognosis (Ferreira et al., 2000; Milo and Snead, 2014).

Current therapeutic approach and treatment options

There are multiple treatment regimens available for TVT. Various approaches, from traditional surgical methods to modern forms of surgery such as electrosurgery and cryosurgery, have shown promising results (Fig. 4 and Table 1). Other therapeutic approaches like radiotherapy, chemotherapy, immunotherapy, and biotherapy have been extensively used (Parikh et al., 2023). Recent chemotherapy protocols include cyclophosphamide, vincristine

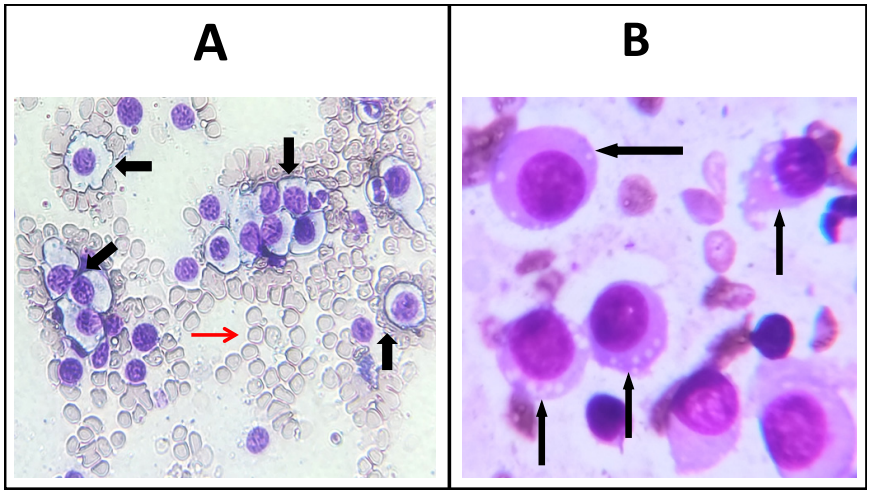

Fig 2: Impression smear prepared from tumour mass (Giemsa staining); (**A**) Mitotic figure in nucleus, irregular cytoplasmic border of tumour cells (Black arrows) and RBCs (Red arrow); (**B**) Cytoplasmic vacuoles in tumour cells and increased nucleus to cytoplasm ratio (Typical findings of Transmissible Venereal Tumour (TVT)

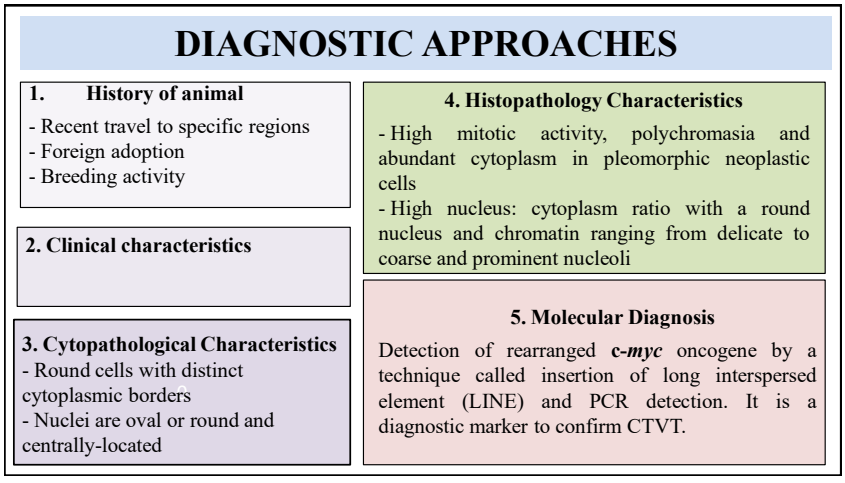

Fig 3: Different diagnostic approaches for Canine Transmissible Venereal Tumour

sulphate, vinblastine, doxorubicin, and methotrexate, used as single agents or in combination. Vincristine sulphate is the most effective and safe treatment in clinical practice, while immunotherapy should use immune-enhancing substances like interleukin-2 (IL2) (Den Otter et al., 2015) and exosomes derived from tumour cells (Ramos-Zayas et al., 2018) in immune-compromised animals (Abedin, 2020).

Vincristine: Advantages, Challenges and Solutions

Vincristine sulphate is a highly effective chemotherapy for treating TVT in dogs, with a 90% success rate and a relatively affordable price (Pooja et al., 2024). Its mechanism of action is to stop cell division or mitosis at the metaphase stage, and it is administered intravenously with saline or isotonic solutions. The tumorous mass stops bleeding 3–4 days after the first shot. The size of the tumour gets drastically reduced after the second shot (Arunpandian et al., 2021). The third shot is given to further diminish the growth, and the animal experiences complete recovery (Filho et al., 2020).

However, administration of vincrystine sulphate is associated with several side effects. Common side effects include neurotoxicity, paresthesia, and constipation, with male dogs experiencing decreased semen quality, which returns within 15 days after the last dose (Cunha et al., 2017). It is also associated with highly elevated aspartate aminotransferase (AST), alkaline phosphatase (ALP), and bilirubin post-treatment (Nazer et al., 2023). If accidentally exposed, vincristine sulphate can cause skin irrita-

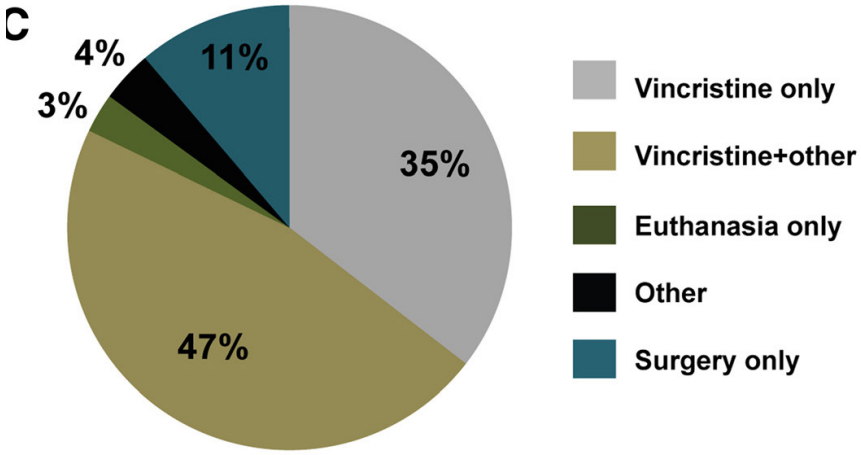

Fig 4: Use of different treatment protocol typically employed for Canine Transmissible Venereal Tumour globally (Strakova and Murchison, 2014).

Table 1: Comparison of various treatment regimens for CTVT

Therapeutic choices	Description
Surgical Interventions	It is crucial for diagnosing and treating solid tumours, but not for diffuse TVT cases. Electrosurgical excision, or cryosurgery, is effective. Conventional surgical methods increase recurrence rates (approximately 30%), but decreased rates can be achieved with a combination of other means of therapy.
Radiotherapy	Radiotherapy, a form of energy ionised by atoms or molecules, is used to treat TVT using orthovoltage and cobalt, with dose recommendations ranging from 1500 to 2500 rads (efficiency is close to 100%). It is recommended for cases where other treatments fail due to practicality issues.
Immunotherapy	TVT can be treated using whole blood or serum transfusions from recovered animals or autochthonous vaccines from tumour tissue homogenates. Bacterial toxins, like Chromobacterium prodigiosum, may also be used. Immunotherapy, including passive immunity and active immunisation, is also used, along with modern approaches using interleukins and viral agents.
Chemotherapy	Chemotherapy is a recommended treatment for TVT cases, including common agents like vincristine sulphate, doxorubicin, cyclophosphamide, vinblastine, methotrexate, and lomustine. Among them, vincristine sulphate is the most effective, safe, and appropriate single-agent therapy with 100% efficacy. However, recent developments in resistance to vincristine and recurrence after vincristine have led to the design and development of newer chemotherapeutic regimens.

tion and necrosis. Extreme cautions like strict intravenous administration and precise dose calculation are needed while administering the drug (Said et al., 2009). There can be life-threatening conditions if the drug is administered without dilution.

Despite having promising results, there are some cases of recurrence and resistance against vincristine. Vincristine resistance is linked to the overexpression of the plasma membrane protein P-glycoprotein, found in various tissues like the kidney, liver, colon, brain, lung, peripheral blood, and bone marrow (Gaspar et al., 2010). Tumours from these tissues exhibit intrinsic resistance to chemotherapy. This particular challenge may be encountered by combining vincristine with ivermectin. Because ivermectin is an antiparasitic drug that uses a P-glycoprotein substrate, it reduces the number of molecules in the tissue (Sewoyo and Kardena, 2022). Though vincrystine sulphate is recommended based on body surface area, whereas in practice it is administered by calculating body weight, the discrepancies thus occurring are shown in Fig. 5.

This graphic (Fig. 5) contrasts the vincristine dosage for a certain body weight (BW) with the BW's corresponding body surface area (BSA). Interestingly, the amount of vincristine is higher when calculated as per BSA than BW until about 24 kg, and after that, the BW curve takes a steep slope to go way beyond the BSA curve. Although the therapeutic response can be achieved by both regimens effectively, it may be concluded that until about 24 kg, vincristine can be given according to BW as it remains lower than the dose according to BSA. This may reduce the risk of overdosing. Similarly, when the BW exceeds 24 kg, the therapeutic dose of vincristine calculated according to BW remains lower as compared to the dose calculated according to BSA. Again, in this scenario, we can consider the lower therapeutic dose (*i.e.*, according to BSA) to avoid the risk of overdosing (Frazier & Price, 1998).

Alternative Chemotherapeutic agents

Alternative chemotherapeutic agents that have been used and validated for treatment include cyclophosphamide, vinblastine, methotrexate, or a combination of these three drugs (Awan et al., 2014). However, case reports have indicated that there is no significant advantage in using a combination of chemotherapy over vincristine injection alone (Amber et al., 1990; Sewoyo and Kardena, 2022). For cases that are resistant to treatment, the treatment regimen may include doxorubicin and lomustine (Uçar, 2016).

Why alternative approach is required?

Resistance: Some tumours may develop resistance to vincristine over time, rendering it ineffective. Alternative treatments may be needed to combat this resistance and continue to effectively treat the cancer.

Side effects: While vincristine can be effective, it also carries the risk of side effects such as gastrointestinal upset, bone marrow suppression, and neurotoxicity. Alternative treatments with different side effect profiles may be considered to minimise these adverse effects while still effectively treating the tumour (Table 2).

Extra Caution: It requires multiple doses, and accidental administration of undiluted vincristine can lead to death or severe health issues. It should always be accompanied by supportive therapy.

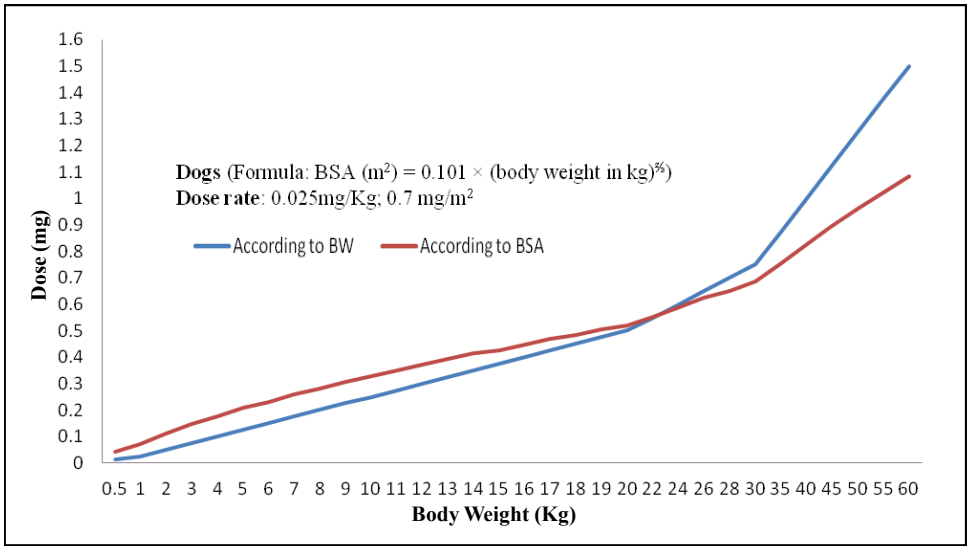

Fig 5: Comparison of therapeutic doses of Vincristine in two different approaches.

Table 2: Comparison of various chemotherapeutic agents used for the treatment CTVT (Sewoyo and Kardena, 2022).

Chemotherapeutic agents	Brief description	Dose rate and route of administration	Side effects
Vincristine Sulfate 1mg/mL 1, 2 mL vial Rs 150/vial (2mL)	Most effective (Drug of choice) 90% success rate Affordable and mild toxicity	0.5-0.7 mg/m² BSA 0.025-0.035 mg/kg BW Strictly I/V, diluted with NS (1:10) Once a week, given two to six weeks until symptoms disappear	Neurotoxicity, paresthesia, constipation Skin irritation, Alopecia (Due to accidental topical application)
Doxorubicin 50 mg/ vial Rs 350/ vial	Belongs to the class of tumour antibiotics Used as alternative therapy to Vincristine resistant cases Effective in most cases	30 mg/m² BSA 1-1.5 mg/kg BW I/V route Continue maximum for 3 weeks	Cardiotoxic effect Arrhythmias Decrease in systolic function
Cyclophosphamide 1000 mg/ vial (IV) Rs 160/ vial 50 mg Tablets (PO) Rs 50/ strip	Alkylating agent Also known as cytophosphane Less effective	50 mg/m² BSA 2.5 mg/kg BW Per oral or I/V route 4 days weekly for 6 weeks(Per Oral) or 2 days weekly for 6 weeks(I/V)	Diarrhoea, liver and kidney damage and a loss of appetite
Vinblastine 10mg/ vial Rs 300/ vial	Analogous to Vincristine Effectiveness is similar to Vincristine but costlier	2.5 mg/m² BSA 0.125 mg/kg BW Strictly I/V Once a week, given two to six weeks until symptoms disappear	Loss of appetite Mild diarrhea Mild haematological changes
Lomustine 40 mg/ capsule Rs 90/ capsule	An alkylating nitrosourea compound Drug of choice in patients of TVT with resistance to Vincristine and heart diseases Cost effective and simple to manage	60 mg/m² BSA 3 mg/kg BW Per oral Weekly once for 3 weeks.	Not much side effects

Lomustine: a potential alternative

It is commonly used to treat mast cell tumours in dogs and may be able to treat brain tumours in dogs because, as previously described, this drug can cross the blood-brain barrier. It has been used in cases of TVT with vincristine resistance. It was first used by Hosoya et al. (2009), along with prednisolone, to treat a case of CTVT. Barboza et al. (2021) used it to treat CTVT, and it resulted in a 100% cure when used alone. There are several other reports also establishing the promising response of this particular drug against TVT (Sewoyo and Kardena, 2022; Costa et al., 2023). A preventive and control measure for CTCT is given in Fig. 6.

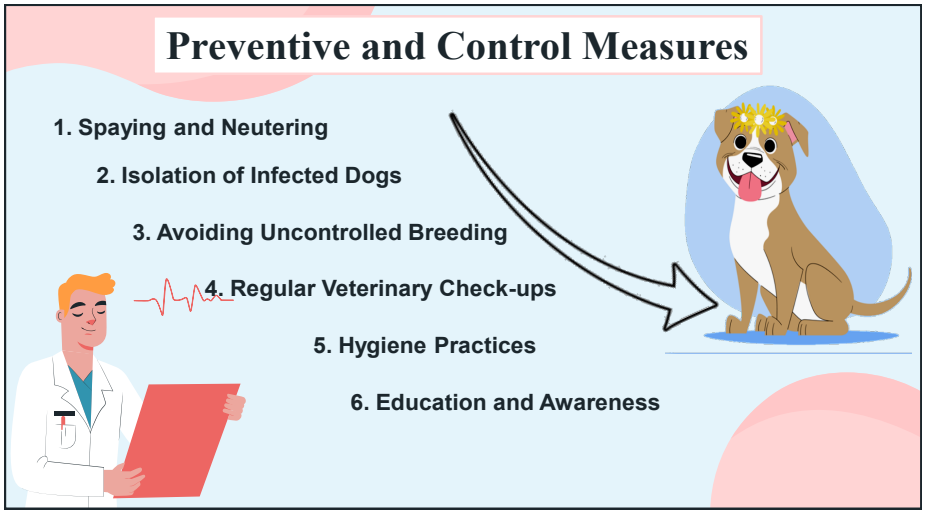

Fig. 6: Some of the important preventive and control measures for Canine Transmissible Venereal Tumour

Risk to humans

Humans are not susceptible to the disease; in fact, even immune-compromised individuals are also not susceptible (Siddle and Kaufman, 2015). But it is always wise to take proper caution and use hand gloves while handling TVT cases. Very interestingly, reports have shown that pet ownership may actually decrease the incidence of cancer in humans (Tranah et al., 2008).

Conclusion

In conclusion, Canine Transmissible Venereal Tumour (CTVT) is a contagious venereal tumour primarily affecting sexually active dogs, with treatment options including chemotherapy, surgery, radiotherapy, and immunotherapy. Recent developments in therapeutic protocols have shown promise in cases resistant to traditional treatments, emphasising the importance of reviewing and reformulating current therapeutic approaches.

Conflict of interest

Author declares no conflict of interest.

Acknowledgements

We would like to express our gratitude to all the contributors for their invaluable assistance and support in the preparation of this review article. Their expertise, feedback, and encouragement have significantly contributed to the quality and coherence of this work. Additionally, we extend our appreciation to the reviewers for their insightful comments and suggestions, which have greatly enhanced the clarity and comprehensiveness of the manuscript.

References

Abedin SN. Canine transmissible venereal tumor: A review. J Entomol Zool Stud. 2020; 8(2): 596-599.

Abeka YT. Review on canine transmissible venereal tumor (CTVT). Ther Oncol Int J. 2019; 14(4): 1-9.

Alkan H, Satilmis F, Alcigir ME, Kivrak MB, Aydin I. Clinicopathological evaluation of disseminated metastases of transmissible venereal tumor in a spayed bitch. Acta Sci Vet. 2017; 45(S1): 1-6.

Amber EI, Henderson RA, Adeyanju JB, Gyang EO. Single-drug chemotherapy of canine transmissible venereal tumor with cyclophosphamide, methotrexate, or vincristine. J Vet Intern Med. 1990;4(3):144-7. Doi: 10.1111/j.1939-1676.1990.tb00887.x.

Arunpandian J, Neethu B, Srivastava N, Kujur A, Aswinisivan G. Successful therapeutic management of canine transmissible venereal tumour in native breed dogs of TamilNadu. Indian J Anim Reprod. 2021; 42(1): 56-57.

Awan F, Ali MM, Ijaz M, Khan S. Comparison of different therapeutic protocols in the management of canine transmissible venereal tumour: Review of 30 cases. Global Vet 2014; 12: 499-503.

Ayala-Díaz S, Jiménez-Lima R, Ramírez-Alcántara KM, Lizano M, Castro-Muñoz LJ, Reyes-Hernández DO, Arroyo-Ledezma J, Manzo-Merino J. Presence of Papillomavirus DNA sequences in the canine transmissible venereal tumor (CTVT). PeerJ. 2019;7:e7962. Doi: 10.7717/peerj.7962.

Barboza AD, Algibay NR, Caorsi CM, Villardino NB, Oribe CA, Brandl S, Gulla AB. Lomustine therapy for vincristine-resistant canine transmissible venereal tumor: a case report. J Vet Med. 2021; 43(1): 1-9.

Bendas AJR, Moreto PLDN, Coxo AB, Holguin PG, Soares DDV. Intra-abdominal transmissible venereal tumor in a dog: a case report. Braz J Vet Med. 2022;44:e001422. Doi: 10.29374/2527-2179.bjvm001422.

Birhan G, Chanie M. A review on canine transmissible venereal tumor: from morphologic to biochemical and molecular diagnosis. Acad J Ani Dis. 2015; 4(3):185-95.

Çizmeci SÜ, Guler M. Transmissible venereal tumour (TVT) in bitches and therapy: a review. Malays J Vet Res. 2018; 9: 136–43.

Costa TS, Paiva FND, Manier BSML, Conceição CLD, Reis AADL, Fernandes JI. Lomustine for treatment of canine transmissible venereal tumor. Ciência Rural, 2023; 53(8): 1-5

Cunha SDS, Silva FBF, Corgozinho KB, da Silva KGC, Ferreira AMR. Adverse effects of chemotherapy in dogs. World Vet J. 2017; 7(3): 74-82.

Das U, Das AK. Review of canine transmissible venereal sarcoma. Vet Res Commun. 2000;24(8):545-56. Doi: 10.1023/a:1006491918910.

Ferreira AJ, Jaggy A, Varejão AP, Ferreira ML, Correia JM, Mulas 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(4):165-8. Doi: 10.1111/j.1748-5827.2000.tb03187.x.

Filho NP, Torres AAA, Silva MPC, Ventura RFA, Basso KM, Ferreira MGPA, Calderón C. Transmissible venereal tumor: cell proliferation (agnor) and response to chemotherapy correlated with cytomorphological classification. Ars Vet. 2020; 36(2): 140-147.

Frazier DL, Price GS. Use of body surface area to calculate chemotherapeutic drug dose in dogs: II. Limitations imposed by

pharmacokinetic factors. J Vet Intern Med. 199812(4):272-8. Doi: 10.1111/j.1939-1676.1998.tb02122.x.

Ganguly B, Das U, Das AK. Canine transmissible venereal tumour: a review. Vet Comp Oncol. 2016;14(1):1-12. Doi: 10.1111/vco.12060.

Gaspar LFJ, Ferreira I, Colodel MM, Brandão CVS, Rocha NS. Spontaneous canine transmissible venereal tumor: cell morphology and influence on P-glycoprotein expression. Turk J Vet Anim Sci. 2010; 34(5): 447-454.

Gonzalez CM, Griffey SM, Naydan DK, Flores E, Cepeda R, Cattaneo G, Madewell BR. Canine transmissible venereal tumour: a morphological and immunohistochemical study of 11 tumours in growth phase and during regression after chemotherapy. J Comp Pathol. 2000;122(4):241-8. Doi: 10.1053/jcpa.1999.0366.

Hosoya K, Kisseberth WC, Alvarez FJ, Lara-Garcia A, Beamer G, Stromberg PC, Couto CG. Adjuvant CCNU (lomustine) and prednisone chemotherapy for dogs with incompletely excised grade 2 mast cell tumors. J Am Anim Hosp Assoc. 2009;45(1):14-8. Doi: 10.5326/0450014.

Jain A, Tiwari RP, Tiwari SK, Gupta N, Awasthi MK. Histopathological studies in canine transmissible venereal tumour. Indian J Anim Reprod. 2002; 23(1): 60-62.

Küçükbekir ÇN, Uçmak ZG, Tek Ç. Canine transmissible veneral tumor: etiology, diagnosis and treatment. J Istanbul Vet Sci. 2021; 5(1): 57-65.

Liao KW, Hung SW, Hsiao YW, 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(3-4):149-62. Doi: 10.1016/s0165-2427(03)00032-1.

Liu CC, Wang YS, Lin CY, Chuang TF, Liao KW, Chi KH, Chen MF, Chiang HC, Chu RM. Transient downregulation of monocyte-derived dendritic-cell differentiation, function, and survival during tumoral progression and regression in an in vivo canine model of transmissible venereal tumor. Cancer Immunol Immunother. 2008;57(4):479-91. Doi: 10.1007/s00262-007-0386-0.

Milo J, Snead E. A case of ocular canine transmissible venereal tumor. Can Vet J. 2014;55(1):1245-9. Erratum in: Can Vet J. 2014;55(2):106.

Nazer AT, Becha BB, Jayakumar C, Unnikrishnan MP, Devi STST. Haemato-biochemical evaluation of chemotherapy in canine transmissible venereal tumour. Indian J Anim Reprod. 2023; 44(1): 23-27.

Den Otter W, Hack M, Jacobs JJ, Tan JF, Rozendaal L, VAN Moorselaar RJ. Effective Treatment of Transmissible Venereal Tumors in Dogs with Vincristine and IL2. Anticancer Res. 2015;35(6):3385-91.

Parikh NP, Panchal MT, Parmar JJ, Ghodasara DJ. Therapeutic management of transmissible venereal tumour in dogs. Indian J Vet Sci. 2023; 19(4): 78-83.

Pooja JK, Bhardwaj V, Dangi A, Kumar P. Transmissible venereal tumor and its successful treatment in canines. Int J Adv. 2024; 8(1S): 753-756.

Priyadarshini N, Das DP, Panda SK, Samal L. Transmissible venereal tumours (TVT) in bitches: A haematological, biochemical and histopathological study. J Entomol Zool Stud. 2021; 9(1): 490-493.

Purohit GN. Canine transmissible venereal tumor: a review. Internet J Veterin Med. 2009; 6(1): 1-10.

Ramos-Zayas Y, Franco-Molina MA, Hernádez-Granados AJ, Zárate-Triviño DG, Coronado-Cerda EE, Mendoza-Gamboa E, Zapata-Benavides P, Ramírez-Romero R, Santana-Krymskaya SE, Tamez-Guerra R, Rodríguez-Padilla C. Immunotherapy for the treatment of canine transmissible venereal tumor based in dendritic cells pulsed with tumoral exosomes. Immunopharmacol Immunotoxicol. 2019;41(1):48-54. Doi: 10.1080/08923973.2018.1533969.

Rebbeck CA, Thomas R, Breen M, Leroi AM, Burt A. Origins and evolution of a transmissible cancer. Evolution. 2009;63(9):2340-9. Doi: 10.1111/j.1558-5646.2009.00724.x.

Said R, Silva L, Albuquerque A, Sousaneta E, Lavinsky M. Efficacy and side effects of vincristine sulfate treatment on canine transmissible venereal tumor. In: Proceeding of the 34th World Small Animal Veterinary association. Brazil 2009; https://www.cabidigitallibrary.org/doi/pdf/10.5555/20103139058.

Sankar P, Ramya R, Ali MG. Therapeutic management of intranasal transmissible venereal tumor in a dog. Intas Polivet, 2016; 17(2): 543-545.

Setthawongsin C, Techangamsuwan S, Rungsipipat A. Canine transmissible venereal tumor: An infectious neoplasia in dogs. In Recent in Advances Canine Medicine. IntechOpen 2022. https://doi.org/10.5772/intechopen.106150.

Sewoyo PS, Kardena IM. Canine transmissible venereal tumor: treatment review and updates. Rev Electron Vet. 2022; 23(1): 01-07.

Siddle HV, Kaufman J. Immunology of naturally transmissible tumours. Immunology, 2015; 144(1): 11-20.

Strakova A, Murchison EP. The changing global distribution and prevalence of canine transmissible venereal tumour. BMC Vet Res. 2014;10:168. Doi: 10.1186/s12917-014-0168-9.

Tranah GJ, Bracci PM, Holly EA. Domestic and farm-animal exposures and risk of non-Hodgkin's lymphoma in a population-based study in the San Francisco Bay Area. Cancer Epidemiol Biomarkers Prev. 2008;17(9):2382-7. Doi: 10.1158/1055-9965.EPI-08-0373.

Uçar M. Transmissible venereal tumor: a review. Kocatepe Vet J. 2016; 9(3): 230-235.