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Canine Transmissible Venereal Tumor

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Abstract

Canine Transmissible Venereal Tumor (CTVT) is a contagious neoplasm which is transmitted between dogs as an allogenic graft. The neoplastic cells originate from normal cell that has undergone tumourigenic transformation as a result of genetic mutations. It is the oldest and most prolific neoplasm lineage known in nature, which evolved 11,000 years. CTVT affects the genital and extra-genital sites of both sexes and is transmitted by allogenic transfer of viable neoplastic cells during coitus or by biting, scratching or licking the affected areas by the transplantation of tumor cells. It is most common in dogs aged 2 to 5 years and the incidence is high in females compared to males. It is homogenously distributed in India and reported in all parts of the world, except Antarctica. CTVT escape from the host immune mechanism by not expressing the MHC molecules on the cell surface. The neoplasm undergoes three different stages includes progressive phase, stable phase and regressive phase. Clinical signs include bloody discharge from the genital region and cauliflower- like growth in the genital region of both sexes. Diagnosis of this tumor by examination of cytology, histopathology and molecular confirmation. Cytology is the gold standard method of diagnosis, in which neoplastic cells are round with oval or round nucleus with one or two nucleoli and cytoplasm have punctuate vacuoles and fine granules. In histopathology, CTVT characteristically presents as a group of compact masses of diffusely arranged round or polyhedral cells with a centrally located nucleus and having punctuate vacuoles in the cytoplasm which are supported by thin trabeculae of fibrovascular tissue. CTVT cells are aneuploid, having stable karyotype of 57–59 chromosomes compared to normal chromosome number of dog. The CTVT cells are marked by the presence of Long Interspersed Nuclear Element (LINE-1) insertion close to the c-myc gene and homozygous loss of the CDKN2A (Cyclin Dependent Kinase Inhibitor 2A) gene.

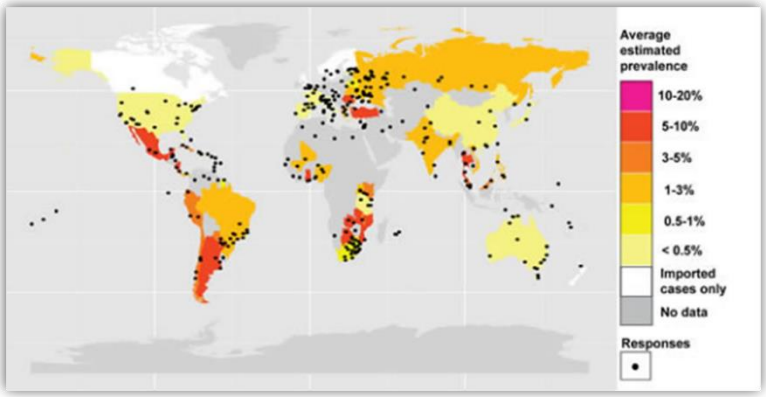
Introduction

Tumor is a disease of genome that arise due to accumulation of mutation in the tumor suppressor gene or proto-oncogene which results in abnormal cell proliferation. Most of the tumors are not contagious and is limited only to the individual that it arises from. However, the canine transmissible venereal tumor (CTVT) is contagious neoplasm with mesenchymal origin and it is transmitted from one host to another as an allogenic graft during copulation. It is also called as canine infectious sarcoma, canine venereal granuloma, canine transmissible lymphosarcoma, canine round cell sarcoma, or canine sticker tumor.

It is commonly observed in dogs that are in close contact with other dogs or in stray and wild dogs that exhibit increased sexual activity. It is the oldest and most prolific neoplasm lineage known in nature, which evolved 11,000 years. CTVT affects the genital and extra-genital sites of both sexes and is transmitted by allogenic transfer of viable neoplastic cells during coitus or by biting, scratching or licking the affected areas by the transplantation of tumor cells.

Epidemiology

CTVT is most common in dogs aged 2 to 5 years and there is no breed or sex predisposition. It has been reported in all the continents of the world except Antarctica. It is more prevalent in tropical and subtropical regions, particularly in the southern United States, Central and South America, south-east Europe, Ireland, China, the Far East, Middle-East and parts of Africa. This tumor is homogeneously distributed across varying geo-climatic zones in India and the prevalence of the disease ranged from 23-28%.



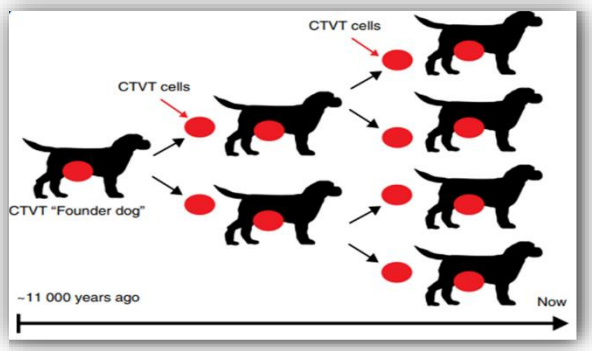
Incidence

Occurrence of tumors in season is highly variable and is correlated with estrus cycle in bitches. Incidence of TVT is more in females when compared to males because male dogs are constantly sexually receptive, have greater opportunity to spread disease, in contrast to female, which become sexually receptive only once every 6-7 months. The age wise incidence was more common in young and adult middle-aged dogs (1- 5 years), because these age group dogs are sexually overactive and hence, are more prone for exposure.

Transmission

The transmission of CTVT may be facilitated by the contact maintained between male and female genital mucosa, which is commonly injured during canid mating and postcoital tie. During copulation the neoplastic cells are transmitted from affected dogs to susceptible dogs as an allogenic graft. These tumors may also occasionally be found in non-genital regions, most commonly skin, nasal cavity, lymph node, eye and mouth by biting, licking and sniffing the affected area. Once the neoplastic cells enter into a new

host, they start to reproduce over a period of two to six months to form a tumour-like growth, usually around the genitals.

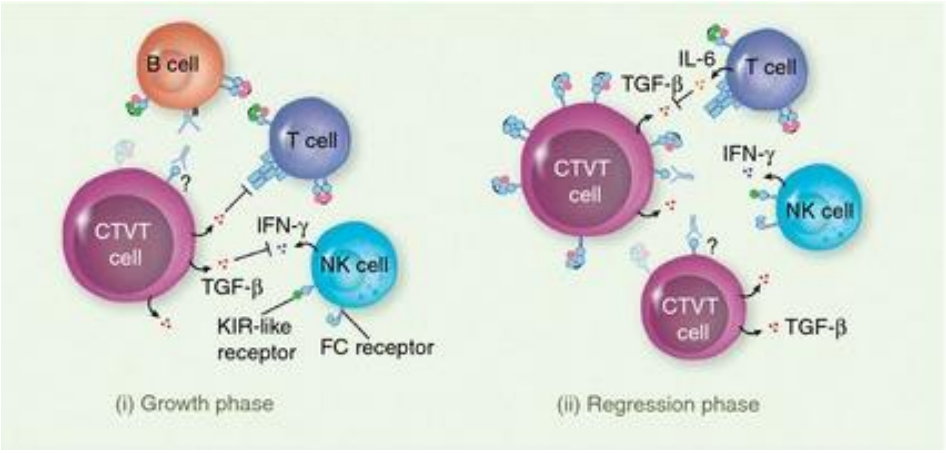


Pathogenesis

In natural and experimental cases, the tumor exhibits three growth patterns that includes progressive phase, static phase and regression phase. During the **progressive phase** (P- phase) the tumor cells evade immune recognition by producing transforming growth factor-1 (TGF-1), and that this cytokine inhibits the activity of natural killer cells (NK) and the infiltration of cytotoxic lymphocytes and decreases MHC expression. Cytotoxic substances produced by the tumor cells cause B-lymphocyte apoptosis during the progression phase.

During **stable phase**, there is markedly slower tumor growth and estimated cell loss of 80- 90%. Following the stable phase, up to 80% of tumor enter a regressive phase during which the tumor shrinks and eventually disappears. During the **regression phase** (R- phase), the number of tumor infiltrating lymphocytes (TILs) increases; these cells secrete interferon-γ (IFN-γ) and interleukin-6 (IL-6) which block the inhibitory effects of tumor derived TGF-1 and induce the expression of MHC in tumor cells.

The expression of MHC in the CTVT triggers the immune system and the regression of the tumor.



Clinical signs

The early signs of the diseases include serous or serosanguineous discharge from the vulva or the prepuce and licking of the affected organs. In early stages of disease, the tumors appears single or multiple small grey- red firm nodules in the male the bulbus glandis, but may also involve the glans penis and the prepuce. In the female, the tumors may develop at any site within the vagina, at later stage, the tumors appears as a cauliflower- like, pedunculated or multilobulated mass which frequently bleeds and ulcerates. It may also develop in extra-genital sites such a such as skin, subcutaneous tissues and around and in the oral and nasal cavities. CTVT rarely metastasizes to other sites.

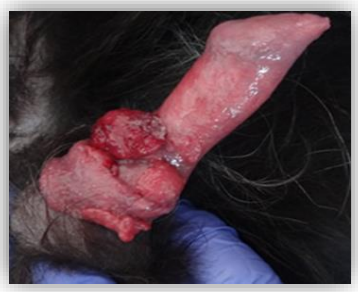


Fig.1. Tumor appears as a single firm nodule in the bulbus glandis.

Fig.2. Tumor appears as a cauliflower- like growth protruded out from vagina.

Fig.3. Tumor appears as a single firm nodule in the conjunctiva of

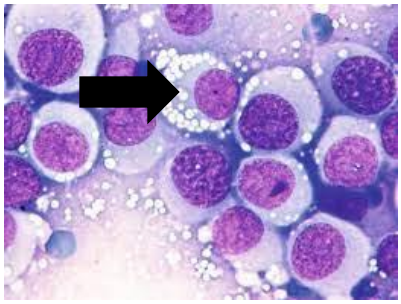
Fig.4. Tumor growth in the gingiva of oral cavity

Fig.5. Multiple tumor growth in the cutaneous site

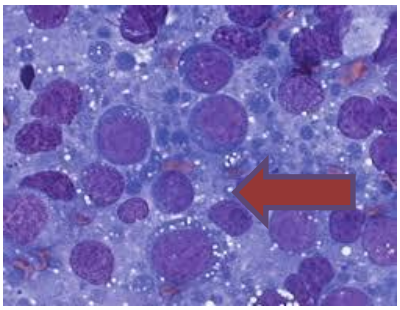
Diagnosis

Cytology: CTVT was classified as cellular, with round cells ranging from 14-30 µm in diameter and arranged in sheets. They contain round to oval nuclei with coarse chromatin arranged in a cord-like pattern. The nucleolus is large and visible and the finely granular cytoplasm is very characteristically vacuolated.

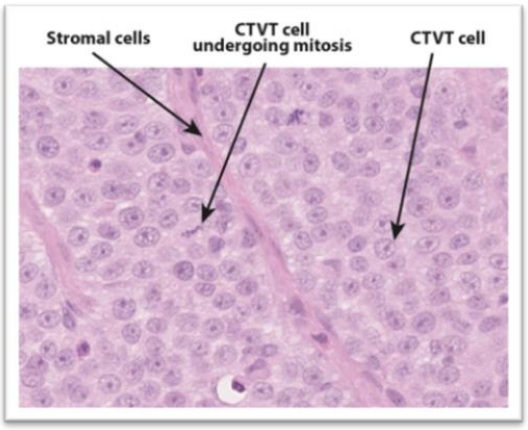
Three sub-types are there namely plasmacytoid, lymphocytoid and mixed. The l**ymphocytic** subtype contains cells with 60% or more round morphology and a scarce and finely granular cytoplasm. Cytoplasmic granules occupy the cell periphery, and cells contain a round nucleus with rough chromatin and one or two prominent nucleoli. **The plasmacytic** subtype contains cells with 60% or more ovoid morphology. The N:C ratio is higher than in the lymphocytic subtype, and the nucleus is eccentrically located. The mixed type contains both lymphocytoid and plasmacytoid, with neither type exceeding 59% of total cells.

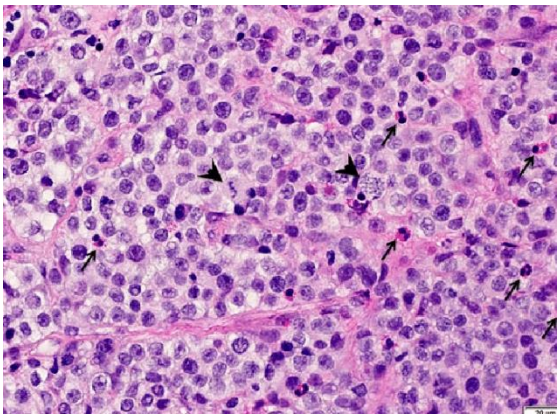


Black arrow-
Plasmacytoid
Brown arrow-
Lymphocytoid



Histopathology: CTVT characteristically presents as a group of compact masses of diffusely arranged cells which are supported by thin trabeculae of fibrovascular tissue. The cells are round or polyhedral with a centrally located, round nucleus containing a prominent nucleolus. The cytoplasm is slightly granular, vacuolated and eosinophilic and generally has indistinct borders.





Special features of CTVT

CTVT cell is aneuploid, but has a repeatable and relatively stable karyotype of 57–59 chromosomes, compared to the canine constitutive karyotype of 78. The CTVT cells are marked by the presence of Long Interspersed Nuclear Element (LINE-1) insertion close to the c-myc gene. The LINE-1 insertion close to c-myc is absent at corresponding position in the germline. This insertion disrupts transcriptional activity of the proto-oncogene c-myc, initiating carcinogenesis. The CTVT also have the

homozygous loss of the CDKN2A (Cyclin Dependent Kinase Inhibitor 2A) gene, which is present in the host cell genome.

Treatment for CTVT

Treatment of this tumors can be achieved through surgery, chemotherapy, radiotherapy, immunotherapy, or a combination of these. Currently the drug of choice for treatment is Vincristine at a dose of 0.025mg/ kg body weight intravenous route, once a week, for 2 weeks beyond resolution of the tumors, irrespective of the neoplasm size and extent, the presence of metastases and the duration of the disease. Other chemotherapeutic agents include cyclophosphamide, doxorubicin, and combinations of these with each other and with prednisone can also been used.

Prevention and control

Presence of free roaming dogs is a high risk of transmission, so it is recommended that owners avoid their dogs to roam freely in the streets. Reproductive control for stray dogs and dogs not intended for breeding is the best way to control this neoplasm.

References

Abeka, Y.T. (2019). Review on canine transmissible venereal tumor (CTVT). *Canc Therapy Oncol. Int. J.*, 14: 555-895.

Cohen D. (1973). The biological behaviour of the transmissible venereal tumour in immunosuppressed dogs. *European J. Cancer.*, 9:253-258

Das, U. and Das, A.K. (2000). Review of canine transmissible venereal sarcoma. *Vet. Res. Commun.*, 24: 545–556.

Ganguly, B., Das, U. and Das, A.K. (2013). Canine transmissible venereal tumour: a review. *Vet. Comp. Oncol.*, 14: 1-12.

Jones, E.A., Cheng, Y. and Belov, K. (2015). The origin, dynamics, and molecular evolution of Transmissible cancers. *Adv. Genomics and Genet.*, 5:317- 326.

Strakova, A and Murchison E. P. (2015) The cancer which survived: insights from the genome of an 11000-year-old cancer. *Curr. Opin. Genet. Dev*., 30: 49-55.