

Case Study of Canine Transmissible Venereal Tumor

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Abstract

Canine Transmissible Venereal Tumor (CTVT) is usually a sexually transmitted neoplasm of the external genitalia of dogs the tumor occurs naturally on the genitals of both male and female dogs. In male dogs it is located on the penis or preputium, and in females is present on the vagina or labia. Even though many treatment aspects are available, here in this case study we mainly deals with chemotherapeutic method of treatment and its effectiveness.

Keywords: Canine Transmissible; Venereal Tumor; Venereal Tumor; TVT

Abbreviations: TVT: Transmissible Venereal Tumor; F/S: Fecal Sample; OD: Once Daily; IV: Intravenously;

Introduction

Canine Transmissible Venereal Tumor (CTVT) is usually a sexually transmitted neoplasm of the external genitalia of dogs. This tumor is unique in oncology because it was the first tumor to be transmitted experimentally, this being achieved by the Russian veterinarian Nowinsky in 1876. Canine Transmissible Venereal Tumor (CTVT) also known as infectious sarcoma, venereal granuloma, transmissible lymphosarcoma or Sticker's sarcoma, this tumor was first reported in 1820 by Huzzard and was then later reported by Delabere-Blaine (1928). However, it was best characterized by Sticker between the years of 1905-1906, leading to its designation as Sticker Tumor for many years. It is a benign reticuloendothelial (histiocytic) tumor of the dog that mainly affects the external genitalia. The tumor occurs naturally on the genitals of both male and female dogs. In male dogs it is located on the penis or preputium, and in females is present on the vagina or labia. Canine transmissible venereal tumors (TVT) are cauliflower-like, pedunculated, nodular, papillary, or multilobulated in appearance [1]. They range in size from a small nodule (5 mm) to a large mass (> 10 cm) that is firm, though friable. The surface is often ulcerated and inflamed and bleeds easily. It is transmitted from animal to animal during copulation. The tumor does not often metastasize except in puppies and immune compromised dogs.

Methods

Five different cases were selected for case study.

Case 1

Dog, Labrador; 4 yr, Female, 30 kg. Reported that animal was in heat, it is showing bleeding for past 20 days. Whelped two months back. It had a regular vaccination & deworming history. Respiration: Panting, Pulse: 82/min, Temperature: 102.3° F, MM: Congested, LN: not palpable. Vulval mucosa was pale. There was no sign of heat. On vulval examination mucosa was pale, mass could be palpated while passing finger through vulva.

Vaginal cytology: TVT cells could be detected. Treatment give

Inj. Cytocristin 1 ml X1

Aqua dist ad 9 ml

Mft inj sig 10 ml IV

Advised

T.Aciloc100mgX7

Sig 1 tab OD

Before food

Advised to continue the treatment after one week. Continued the treatment for four weeks.

Case 2

Dog, Labrador, 7 yr, Female, 20 kg. Reported that animal is having a mass over perineal region. Animal is weak. It had a regular vaccination & deworming history. Whelped one year back. Respiration: 20/min, Pulse: 76/min, Temp: 102.1° F, MM: Congested, LN: not palpable, Huge tumor mass was hanging through vulva. On examination large tumor mass could be seen hanging through vulva, while passing finger through vulva more tumor mass could be palpated.

Vaginal Cytology: TVT cells was observed. Treatment given

Inj atropine 1 ml X1

Sig 1ml IM

Inj xylaxin 10 ml X 1

Sig 1.5 ml IM

Inj Aneket 10 ml X1

Sig 1.5 ml IM

Under general anesthesia, tumor mass was removed after ligating the blood vessels.

Given

Inj Cytocristin 1 ml X1

Aqua dist ad 9 ml

Mft inj sig 10 ml IV

Advised to continue the treatment after one week. Continued the treatment for four weeks.

Case 3

Dog, Rottweiler, 3 yr, Female, 25 kg, Reported that animal is having a mass over perineal region. Animal is active. It had a regular vaccination & deworming history. Whelped six month back. Respiration: 23/min, Pulse: 82/min, Temp: 102.3° F, MM: Congested, LN: not palpable. Huge tumor mass was protruding through vulva. On examination large tumor mass could be seen protruding through vulva, finger was not able to through vulva, to palpate more tumor mass. Treatment given

Inj. Cytocristin 1 ml X1

Sig 0.5 ml IV

Along with 5ml distilled water

Advised

T. Rantac 100 mg X7

Sig 1 tab OD

Before food

Advised to continue the treatment after one week. Continued the treatment for four weeks.

Case 4

Dog, Pug, 6 yr, Female, 15 kg, Reported that animal is showing bleeding for more than 20 days It had a regular vaccination & deworming history. Whelped eight month back. Respiration: 20/min, Pulse: 82/min, Temp: 101.3° F, MM: Pale, LN: not palpable. Animal is active. F/S: No parasitic ova could be detected. On passing finger through vulva, a cauliflower like growth could be detected.

Vaginal Cytology: TVT cells was observed. Treatment given

Inj. Cytocristin 1 ml X1

Sig 0.5 ml IV

Along with 5 ml distilled water

Advised

T. Rantac 100 mg X7

Sig 1 tab OD

Before food

Advised to continue the treatment after one week. Continued the treatment for four weeks.

Case 5

Dog, Spitz, 3yr, Female, 15 kg, Reported that animal is showing bleeding for more than 15 days. It had a regular vaccination & deworming history. Whelped seven month back. Respiration: 23/min, Pulse: 70/min, Temp: 102.3° F, MM: Pale roseate, LN: not palpable.

Animal is weak. On passing finger through vulva, a cauliflower like growth could be detected.

Vaginal Cytology: TVT cells was observed. Treatment given

1 Inj. Cytocristin 1 ml X1

Sig 0.5 ml IV

Along with 5 ml distilled water

Advised

T. Rantac 100 mg X7

Sig 1 tab OD

Before food

Advised to continue the treatment after one week. Continued the treatment for four weeks.

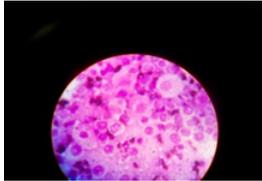
Case 1

Dog, Labrador, 4 yr, Female,
30 kg



<p>Case 2 Dog, Labrador, 7 yr, Female, 20 kg</p>	
<p>Case 3 Dog, Rotweiler, 3 yr, Female, 25 kg</p>	
<p>Case 4 Dog, Pug, 6 yr, Female 15 kg</p>	
<p>Case 5 Dog, Spitz(cross), 3 yr, Female 15 kg</p>	

Table 1: Table showing details of animals selected for case study with images taken when brought for examination.

SIGNALMENT HISTORY OWNER'S COMPLAINT	OBSERVATION	DIAGNOSTIC EXAMINATION, TENTIVE DIAGNOSIS	TREATMENT
<p>CASE 1 Dog, Labrador, 4 yr, Female, 30 kg O/c: Reported that animal was in heat, it is showing bleeding for past 20 days. Whelped two months back. It had a regular vaccination & deworming history.</p>	<p>Respiration: Panting Pulse: 82/min Temperature: 102.3°F MM : Congested LN : not palpable</p> <p>Vulval mucosa was pale. There was no signs of heat</p>	<p>On vulval examination mucosa was pale, mass could be palpated while passing finger through vulva. Vaginal cytology: TVT cells could be detected</p>  <p>Tentative Diagnosis: Transmissible Venereal Tumor</p>	<p>Given 1) Inj. Cytocristin 1 ml X1 Aqua dist ad 9 ml Mft inj sig 10 ml IV Advised T. Aciloc 100 mg X7 Sig 1 tab OD Before food Advised to continue the treatment after one week</p> 
<p>Case 2 Dog, Labrador, 7 yr, Female, 20 kg O/C: Reported that animal is having a mass over perineal region. Animal is weak. It had a regular vaccination & deworming history. Whelped one year back.</p>	<p>Respiration: 20/min Pulse: 76/min Temp: 102.1°F MM : Congested LN : not palpable Huge tumor mass was hanging through vulva</p>	<p>On examination large tumor mass could be seen hanging through vulva, while passing finger through vulva more tumor mass could be palpated Vaginal Cytology: TVT cells was observed Tentative Diagnosis: Transmissible Venereal Tumor</p>	<p>Given Inj atropine 1 ml X 1 Sig 1 ml IM Inj xylaxin 10 ml X 1 Sig 1.5 ml IM Inj Aneket 10 ml X1 Sig 1.5 ml IM Under general anesthesia, tumor mass was removed after ligating the blood vessels. Given Inj Cytocristin 1 ml X1 Aqua dist ad 9 ml Mft inj sig 10 ml IV Advised to continue the treatment after one week</p> 

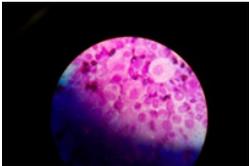
<p>Case 3 Dog, Rottweiler, 3 yr, Female, 25 kg O/C: Reported that animal is having a mass over perineal region. Animal is active. It had a regular vaccination & deworming history. Whelped six month back.</p>	<p>Respiration: 23/min Pulse: 82/min Temp: 102.3°F MM : Congested LN : not palpable Huge tumor mass was protruding through vulva</p>	<p>On examination large tumor mass could be seen protruding through vulva, finger was not able to through vulva, to palpate more tumor mass. Tentative Diagnosis: Transmissible Venereal Tumor</p>	<p>1) Inj. Cytocristin 1 ml X 1 Sig 0.5 ml IV Along with 5ml distilled water Advised T. Rantac 100 mg X 7 Sig 1 tab OD Before food Advised to continue the treatment after one week</p>
<p>Case 4 Dog, Pug, 6 yr, Female 15 kg O/C: Reported that Animal is showing bleeding for more than 20 days It had a regular vaccination & deworming history. Whelped eight month back.</p>	<p>Respiration: 20/min Pulse: 82/min Temp: 101.3°F MM : Pale LN : Not palpable Animal is active.</p>	<p>F/S: No parasitic ova could be detected. On passing finger through vulva, a cauliflower like growth could be detected. Vaginal Cytology: TVT cells was observed</p>  <p>Tentative Diagnosis: Transmissible Venereal Tumor</p>	<p>1) Inj. Cytocristin 1 ml X 1 Sig 0.5 ml IV Along with 5 ml distilled water Advised T. Rantac 100 mg X 7 Sig 1 tab OD Before food Advised to continue the treatment after one week</p>
<p>Case 5 Dog, Spitz, 3 yr, Female 15 kg O/C: Reported that Animal is showing bleeding for more than 15 days It had a regular vaccination & deworming history. Whelped seven month back.</p>	<p>Respiration: 23/min Pulse: 70/ min Temp: 102.3°F MM : Pale roseate LN : Not palpable Animal is weak</p>	<p>On passing finger through vulva, a cauliflower like growth could be detected. Vaginal Cytology: TVT cells was observed Tentative Diagnosis: Transmissible Venereal Tumor</p>	<p>1) Inj. Cytocristin 1 ml X 1 Sig 0.5 ml IV Along with 5ml distilled water Advised T. Rantac 100 mg X 7 Sig 1 tab OD Before food Advised to continue the treatment after one week</p>

Table 2: Table showing history, observation examination details, diagnosis with images taken from vaginal cytology through microscope and treatment protocol followed.

Results and Discussion

Transmission and etiology

CTVT is usually transmitted to genital organs during sexual intercourse but can affect the skin via the direct implantation of tumor cells during contact between skin and tumor masses. Transplantation occurs when intact host tumor cells lose the expression of major histocompatibility complex (MHC) class I and II molecules, enabling transposition of the tissue to a healthy animal by contact between skin and damaged mucosa [2].

Other studies have established that CTVT cells can be derived following mutations induced by viruses, chemicals or radiation of lymphohistiocytic cells and that these clones of tumor cells can then be disseminated by allogenic transplantation. Murgia, *et al.* (2009) and Rebbeck, *et al.* (2009) confirmed the clonal transmission of this tumor when they found that the pattern of microsatellite polymorphisms in CTVT from different regions of the world showed evidence of monophyletic origin. Studies say that CTVT probably arose from a single wolf approximately 7,800 to 78,000 years ago. More recently, a single clone became dominant and then divided into two groups with a worldwide distribution [3,4].

Clinical and pathological characteristics

CTVT commonly affects the external genitalia in dogs of both sexes. In males, the tumor is commonly located in the caudal part of the penis, the glans, and occasionally in the foreskin. In females, this tumor is often found at the junction of the vestibule and the posterior region of the vagina and occasionally in the urethral opening. CTVT can occur as a solitary mass or as multiple tumors with pendular, nodular, papillary or multilobular forms presenting a cauliflower-like appearance. The tumor is friable and is often ulcerated and inflamed. The tumor size can vary from 3 to 12 cm in diameter. Clinical signs of genital CTVT are bloody vaginal or preputial discharge, intermittent or persistent ulcerative skin lesions, poor penile exposure, genital swelling and excessive licking of the genital area [5]. CTVT may also develop in extra-genital sites such as skin, subcutaneous tissues and around and in the oral and nasal cavities. Extra-genital tumors are well circumscribed and can measure 2-5 cm. Metastases are rare in CTVT, yet they can occur, especially in puppies and immune compromised dogs. These metastases are often considered mechanical extensions of the primary tumor; however, metastases have been reported in inguinal lymph nodes, liver and eye.

Histologically, CTVT is composed of round cells, arranged or grouped in strings, interspersed with delicate conjunctival stroma when stained with hematoxylin and eosin. The tumor cells are usually arranged radially around blood and lymphatic vessels and have a high nucleus: cytoplasm ratio with a round nucleus and chromatin ranging from delicate to coarse and prominent nucleoli. These cells contain a large amount of cytoplasm that is slightly acidophilic with poorly-defined limits. Cytological examination reveals the typical round to slightly polyhedral cells, with rather eosinophilic vacuolated thin cytoplasm and a round hyperchromatic nucleus with a nucleolus and a moderate number of mitotic figures. The nucleus to cytoplasmic ratio is large.

Diagnosis

Because of their homogenous populations of large, round cells with distinctive centrally located nucleoli, TVT are usually easily diagnosed by cytologic examination of fine-needle aspirates or impression smears or by histopathologic evaluation of biopsies. TVT may be difficult to distinguish from other round cell tumors, particularly lymphosarcomas, when they occur in extragenital locations. Although TVT has a worldwide distribution, prevalence varies from relatively high in some geographic regions (eg, tropical and subtropical urban environments) to rare in others.

Clinical signs vary according to the localization of the tumors. Dogs with genital localization have a hemorrhagic discharge. In males, lesions usually localize cranially on the glans penis, on preputial mucosa or on the bulbus glandis. Tumoral masses often protrude from the prepuce and phimosis can be a complication. The discharge can be confused with urethritis, cystitis, or prostatitis. The involvement of regional lymph nodes is frequent in males with large tumors. In bitches the tumors are of similar gross appearance as in male dogs and can be localized in the vestibule and/or caudal vagina, protruding from the vulva and frequently causing a deformation of the perineal region. Only very rarely, however, do they interfere with micturition. A considerable hemorrhagic vulvar discharge may

occur and can cause anemia if it persists. The discharge can attract males and the condition of the bitch can be mistaken for estrus by the owners. Infrequently, TVTs can localize in the uterus. In cases with extra genital localization of the TVT, clinical diagnosis is usually more difficult because TVTs cause a variety of signs depending on the anatomical localization of the tumor, e.g., sneezing, epistaxis, epiphora, halitosis and tooth loss, exophthalmos, skin bumps, facial or oral deformation along with regional lymph node enlargement. Definitive diagnosis is based on physical examination and cytological findings typical of TVT in exfoliated cells obtained by swabs, fine needle aspirations or imprints of the tumors [6].

Treatment

Several treatments including surgery, radiotherapy, immunotherapy, biotherapy and chemotherapy have been applied for TVT. Surgery has been used extensively for the treatment of small, localized TVTs, although the recurrence rate can be as high as 50-68% in cases of large invasive tumors. Contamination of the surgical site with TVT cells is also a source of recurrence. Transmissible venereal tumors are radiosensitive and orthovoltage as well as cobalt have been used for this purpose. Biotherapy studies have also been reported. The intratumoral application of Calmette-Guerin's bacillus (BCG) was used for three weeks with sporadic success [8]. Recurrences have been described after immunotherapy using Staphylococcus protein A, BCG or a vaccine made from tumoral cells. Biotherapy has unfortunately also resulted in a high rate of recurrence. Chemotherapy has been shown to be the most effective and practical therapy, with vincristine sulfate being the most frequently used drug. Vincristine (Oncovin®, Lily), is administered weekly at a dose of 0.5 to 0.7 mg/m² of body surface area or 0.025 mg/kg, IV. The involution of the lesions is gradual, although it is particularly noticeable and significant at the beginning of the treatment. Complete remission usually takes 2 to 8 injections and occurs in more than 90% of the treated cases (unpublished observation). A cure rate approaching 100% is achieved in cases treated in the initial stages of progression, especially in cases of less than 1 year duration, and independent of the presence or not of metastases. In cases of longer duration, longer periods of therapy are required, and the cure rate is lower. Side effects can be expected. Cytostatic agents, such as vincristine, can cause myelosuppression and gastrointestinal effects resulting in leukopenia and vomiting in 5 to 7% of the patients. Paresis has also been described as a side effect due to peripheral neuropathy. A complete white blood cell count is, therefore, recommended prior to each administration. When the white blood cell count is below 4,000 mm³ further administration should be delayed 3 to 4 days and the dose of vincristine can be reduced to 25% of the initial dose. The most frequent complication of vincristine treatment is the occurrence of local tissue lesions caused by extravasation of the drug during IV application resulting in the development of necrotic lesions with crusts. Other chemotherapeutic agents indicated for TVT treatment include cyclophosphamide (5 mg/kg, PO, for 10 days as a single drug therapy or given in association with prednisolone, 3 mg/kg, for 5 days); also, weekly vinblastine (0.1 mg/kg, IV during 4 to 6 weeks), methotrexate (0.1 mg/kg, PO, every other day) or a combination of the 3 drugs. However, there is no apparent advantage in the combination of chemotherapy over using vincristine alone. Resistant cases can be treated with doxorubicin (Adriamycin®, Adria Lab, 30 mg/m², IV, with 3 applications every 21 days). When total disappearance of the tumor cannot be achieved by chemotherapy, electro-cauterization or cryo-cauterization can be useful [7]. After therapy, small remnant lesions can disappear spontaneously after 1 or 2 weeks (unpublished observations). In cases that fail to resolve with chemotherapy, radiotherapy has been reported to yield good results.

Conclusion

Since the dawn of civilization, dog is considered as a most trusted companion animal of human being. Now a day's dogs are the modern status symbol of a society. Owners take pride and pleasure in flaunting them. Also man adopts dog breeding as a source of income; CTVT is a great threat to this.

TVT may be solitary or multiple and are almost always located on the genitalia. The tumor is transplanted from site to site and from dog to dog by direct contact with the mass. They may be transplanted to adjacent skin and oral, nasal, or conjunctival mucosa. The tumor may arise deep within the preputial, vaginal, or nasal cavity and be difficult to see during cursory examination. This may lead to misdiagnosis if bleeding is incorrectly assumed to be hematuria or epistaxis from other causes. Initially, TVT grow rapidly and more rapidly in neonatal and immunosuppressed dogs. Metastasis is uncommon (5%) and can occur without a primary genital tumor

present. When metastasis occurs, it is usually to the regional lymph nodes, but kidney, spleen, eye, brain, pituitary, skin and sub cutis, mesenteric lymph nodes, and peritoneum may also be sites. Treatment with vincristin has brought great results. Here all the five dogs make remarkable improvement in condition. General health status of animal should be ensured during the course of therapy. Before therapy is instituted the owner must be made aware of the intensity of treatment and its side effects. They should also be made aware that regular re-examinations of the dog will be necessary, and that adjustments to the treatment may be necessary in the light of those examinations.

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