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REVIEW OF CANINE TRANSMISSIBLE VENEREAL TUMOR WITH A CASE STUDY IN NEPAL

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ABSTRACT

Canine transmissible venereal tumor (CTVT) is frequently reported in dogs and is responsible for high morbidity rates and economic losses. CTVT is considered as the oldest cancer in the world which is nowadays widely distributed worldwide and it is endemic in at least 90 countries. Presence of free-roaming dogs is associated with increased CTVT prevalence. In the present study, it is tried to establish the therapeutic effect of treatment with vincristine sulphate. Five females and five males diagnosed with CTVT based on case history, clinical findings and hematological examination were treated by surgical removal, or chemotherapy or a combination of both in Central Referral Veterinary Hospital (CRVH) Kathmandu, Nepal. The dogs were treated with Vincristine sulphate intravenously at a dose of 0.025 mg/kg at weekly intervals for 2-4 injections and recovered fully within 4 weeks. Interestingly, all ten dogs with chemotherapy were found in good health and no tumor recurrence was noted after 90 days of treatment. Treatment of CTVT with vincristine sulphate appears to have impressive therapeutic effect.

Keywords: CTVT, Free-roaming, Chemotherapy, CRVH, Vincristine sulphate, Prevalence, Recurrence

INTRODUCTION

Tumor is an uncoordinated excessive proliferation of cells without useful function. Transmissible venereal tumors (TVT) are tumors that arise from histiocytes, the dysregulated growth of cells. Histocytes are a type of immune system cells found in many areas of the body, including the skin. TVTs are developed from skin histiocytes. TVTs are malignant cancerous tumors. It is sexually transmitted through direct skin-to-skin contact with the tumor that results in cancer cells being transplanted from dog to dog. This type of tumor is more commonly seen in tropical and subtropical areas, particularly in Central/South American, the southern United States, Asia, and Africa, though it does occur world-wide., Though it is most commonly observed in mixed-breed dogs, all breed, age, or sex are equally susceptible to TVTs that are not neutered, stray and free-roaming dogs [1].

There are many synonyms for Canine transmissible venereal tumor (CTVT). They are known as Sticker's sarcoma, Sticker tumor, transmissible venereal tumor (TVT), contagious venereal tumor, transmissible lymphosarcoma, transmissible ve

nereal sarcoma, venereal granuloma, infectious granuloma, canine condyloma, infectious sarcoma and contagious lymphosarcoma [2]. Canine transmissible venereal tumor (TVT) is a horizontally sexually transmitted venereal round cell tumor [3].

The tumor may arise deep within the preputial, vaginal, or nasal cavity and be difficult to see during superficial examination. This may lead to misdiagnosis if bleeding is incorrectly assumed to be hematuria or epistaxis from other causes. Initially, TVTs grow rapidly, and more rapidly in neonatal and immunosuppressed dogs. Generally, metastasis is uncommon (5%) and can occur without a primary genital tumor. When metastasis occurs, it is usually in the regional lymph nodes, but kidney, spleen, eye, brain, pituitary gland, skin and subcutis, mesenteric lymph nodes, and sometimes peritoneum [4]. One of the consequences of tumoral malignancy is a gradual loss of the patient's weight, a condition that may deteriorate to the state of cachexia. Dogs with this disease experience pain, hemorrhages and exhibit serosanguineous discharge in the external genitalia which is usually cauliflower like in appearance, friable, and red to flesh colored [5].

Emergence of CTVT

Canine transmissible venereal tumor (CTVT) in dogs present a classical example of mitochondrial transfer in vivo. CTVT, the oldest cancer known in world is an infectious cell line circulating in many dog populations, was originated about 11,000 years ago [6]. All CTVT tumors carry the DNA belonging to this "founder dog". The phenomenon of selective sweeping happens over and over in a tumor's early life cycle to make it more and more aggressive. There are more than 200 known driver genes in humans, the genes that when mutated increase cancer cell fitness. In CTVT, it is found only five such mutated driver genes and CTVT cells are riddled with mutations, an average of 38,000 per tumor sample during the emergence of cancer [7].

Current Situation

Factors influencing CTVT prevalence showed that presence of free-roaming dogs was associated with increased CTVT prevalence, while dog spaying and neutering were associated with reduced CTVT prevalence. CTVT is endemic in at least 90 countries worldwide [8]. In Kathmandu Valley there are an estimated 7,500 infected dogs and this number grows month by month. Why this cancer is spreading so rapidly through the stray dog population in Nepal is due to many years of unchecked breeding and lack of systematic health screening for stray dog population [9].

Distribution Pattern

This disease is mostly observed in free-roaming, sexually active dogs in tropical and subtropical countries. CTVT has been reported from all continents of the world except Antarctica [10]. Though there is less reporting from Europe and North America, CTVT remains enzootic in the rest of the world and more problematic in parts of south and central America as well as Africa and Asia where uncontrolled dog breeding is existing with prevalence rate from 1 to 10 percent [8].

Transmission

The tumors are usually transmitted from one dog to another during mating when abraded mucosa is exposed to the tumor of an infected dog [11]. Venereal transmission is the most common way of infection, but it can be transplanted to other sites such as the nose or mucosa of the mouth and transmitted to other dogs by licking, biting, or contact with the tumor [12; 13]. The tumors grow mainly on the genitals. Initial lesions are superficial, pink to red, and 1-3 mm in diameter. Subsequently, multiple nodules fuse together forming larger, red, hemorrhagic, cauliflower-like, friable masses of up to 5-7 cm in diameter and progress deeper into the mucosa as multilobular lesions with diameters 10-15 cm [14]. Adult canines are mostly affected and it does not have sex or breed-specific predisposition. The incidence of this disease is

more restricted to the age of greatest sexual activity and in countries where canine population is not subject to a strict epidemiological control. Females are infected more often than males [15]. The tumors have soft and friable consistency that easily bleeds. The surface is usually inflamed, hemorrhagic, ulcerated and infected. In female dogs, CTVT is most frequently found in the vestibule and less commonly in the vagina [16]. All TVTs have the same chromosomal aberration: whereas normal cells of dogs contain 78 chromosomes, cells from TVTs have 57-59 chromosomes [17].

Treatment

Treatment should be pursued as soon as possible, both to avoid the transfer of the disease to other dogs and to minimize the risk of metastasis. Complete surgical excision, radiotherapy and chemotherapy are effective treatments. Although radiation therapy has been shown to be effective against transmissible venereal tumor [1], it is not easily accessible in veterinary facilities everywhere. Therefore, chemotherapy is considered the treatment of choice. Complete surgical excision may be difficult due to the location and proliferation of tumors. Surgery alone often leads to recurrence. The sequel for total remission with chemo-radiotherapy is found to be effective [1; 18]. This study is focused for CTVT treatment with chemotherapy and if required, surgical excision.

Surgical Excision

Surgery for CTVT is not a good approach because it is impractical in some regions of the body and might be invasive in cases where the tumor size is large [10], with risks of reinfection during removal. It is estimated that 50–68% of relapses occur due to the transplantation of tumor cells into the surgical wound during traditional surgery [16]. With surgery, the recurrence rate is frequent and ranges from 12% to 68% [19; 20]. As CTVT can be easily transplanted into the surgical areas when conventional surgical methods are used, so electrosurgery or cryosurgery may be a better alternative to conventional surgery [16]. The complete surgical removal of large sized localized tumors is done during the treatment. Surgical excision may be curative in dogs with stage I of the disease with non-invasive and non-metastatic involvement. Complete surgical excision, and chemotherapy with vincristine sulfate (0.5 mg/m^2) IV once weekly for 3-6 weeks is effective [21]. In some cases, complete surgical excision cannot be achieved because of the anatomic location of tumors. Unless adjunct radiation or chemotherapy is used, recurrence is likely in such cases [22].

Chemotherapy

Chemotherapy has been shown to be the most effective and practical therapy. There are many antimitotic drugs for the treatment of CTVT, such as cyclophosphamide, methotrexate, vincristine, vinblastine or doxorubicin, however vincristine sulphate is the most frequently preferred drug because of its high effectiveness, low cost, and mild toxicity [23; 24]. Vincristine sulphate belongs to a group of medications known as vinca alkaloids and is obtained from the plant *Vinca rosea* Linn. It acts by interrupting microtubule assembly required for mitotic spindle formation during metaphase and is strictly administered intravenously with saline (24; 25). Single agent therapy with vincristine sulphate is the most effective, safe, and appropriate chemotherapy, resulting in cure even in patients with extra genital metastasis [26; 27]. 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 in the absence of metastases. The cure rate might be lower in cases of later stage tumor as it requires longer periods of therapy [28].

The use of the drug has to be strictly limited to severe dogs only as there are some side effects of vincristine sulphate that include a reduction in appetite, vomiting, and occasional diarrhea. Side effects of vincristine typically occur in the first 24-72 hours after treatment [29]. The side effects are marked by the thrombocytopenia, anemia and leucopenia [30]. Therefore, dose calculation on the basis of body weight measurement has significant importance to minimize its side effects and to increase its effectiveness.

Case Study

Five female and five male dogs at Central Referral Veterinary Hospital, Kathmandu, Nepal were studied separately for the treatment of CTVT. The mean ages of female and male were 4.58±1.52 and 6.00±1.88 respectively. The history revealed a slight decrease in appetite, weight loss, infertility, and progressive cauliflower like tumorous vaginal growth in females, and fresh blood oozing from the prepuce of the male. One of the male had blood in urine regularly. Duration of illness was more than 2 months in both sexes. The clinical examination revealed anemia, weight loss, and fleshy hyperemic, cauliflower like growth on the vulva and vagina of females (Fig. 1 and 2), and similar growth was found on the prepuce area of the penis of the affected male (Fig. 3). The grown areas were quite friable and bleed easily on manipulation. The diagnosis was strongly based on the history, clinical findings and hematological examination. Hematological examinations showed a decrease in the value of red blood cells, hemoglobin and slight increase in lymphocytes in some cases. The cases were treated with intravenous injections of Vincristine at the dose rate of 0.025 mg/kg once a week for 2-4 times. The drug was diluted in 2 ml of normal saline and administered @ 0.5 ml/10 kg body weight in I/V infusions slowly over half an hour.


Fig.1


Fig.2


Fig.3

The treatment with Vincristine sulphate is found satisfactory. The female dogs showed complete regression after 3-4 injections, while the male dog was cured after 1-2 injections. For chronic and later stages tumors, the treatment was extended for 6 weeks and the results were complete remission of the tumor. Interestingly, all dogs remained in good health condition with no evidence of tumor recurrence even after 90 days was noted.

Conclusion and Recommendation

CTVT is a naturally occurring tumor transmitted from animal to animal during copulation by viable tumor cells that mainly affects genital organs. It responds generally well to treatment and dogs that undergo spontaneous regression become immune to future tumor recurrence. In Nepal, CTVT is the most prevalent neoplasia of the external genitalia of the dogs. Due to its dominancy among stray dog populations, the disease is highly transmissible in nature among dogs and its ability to transfer to other wild candidate such as foxes, jackals and coyotes. In Nepal, the management of CTVT is found to be challenging as it is costly for surgical or chemotherapeutic treatment. Current treatment practice is done by using Vincristine sulphate as chemotherapy and surgical intervention is not initiated unless the tumor size is manageable. Since stray dogs serve as a reservoir of CTVT, control is difficult without controlling free-roaming community dogs. Therefore, further study for assessment of prevalence of CTVT has to be done. There is a need of government policy and programs for the control of stray dog population that will definitely contribute for the control of CTVT.

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