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Occurrence of transmissible venereal tumour (TVT) in high altitude of Himalayas and effectiveness of vincristine therapy

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Abstract

Transmissible venereal tumors (TVTs) are tumors that are transmitted between male and female dogs by exchanging body cells through sexual intercourse. Cancer can spread to different parts of the body by smelling, licking, scratching or biting the affected part. This phenomenon can also be seen in wild canines. In female dogs TVT is usually located on the posterior wall of the vagina, at the junction between the vestibule, at caudal end of the penis in male dogs. Initially, the tumor is small, pink to red in color, and then grows into a large, ulcerated infection. At this time the tumor grows, and the disease becomes brittle, engorged, hemorrhagic, multi-lobular and cauliflower shaped. Serum-like vaginal discharge is observed. This study aimed to assess the occurrence of TVT in Himalayan Dogs and Effect of vincristine chemotherapy. Total 40 dogs (20 Male, 20 Female) were investigated. Diagnosis of TVT was based on Cytological Method by using Giemsa staining. Identification of cells was done using compound microscope. TVT round cells were observed in total 37 dogs (92.5%) 19 Female and 18 males. TVT positive dogs were treated with Vincristine Sulphate @ dose rate 0.025 mg/kg intravenous once weekly. 3 dogs (1 Female, 2 male) cured after first dose. 15 Dogs (8 female, 7 male) cured after 2 doses. 12 Dogs (5 Female, 7 male) cured after 3 doses. 4 Dogs (2 Female, 2 male) fully recovered using fourth dose of vincristine. 3 female dogs were treated with 5th dose but not successfully recovered.

Keywords: Transmissible venereal tumors, Himalayan dogs, vincristine, cytological examination

Introduction

TVT, also known as infectious sarcoma, granuloma venereum, infectious lymphosarcoma (Oruc *et al.*, 2011; Erer and Kiran, 2000) [18, 4]. It is a benign reticuloendothelial tumor that mainly affects the mucous membrane of the external genitalia and is rarely seen in internal reproductive organs of both sex (Sankar ve ark, 2016; VonHoldt and Ostrander, 2006; Katzir *et al.*, 1985) [24, 27, 10]. TVT is commonly found in sexually active stray animals in tropical and subtropical regions. (Oruc *et al.*, 2011; Nak *et al.*, 2005; Das and Das, 2000) [18, 16, 3]. According to the report 44.1% of tumors found in dogs in genitalia and 14.7% of these are venereal tumors. (Erer and Kiran 1993) [4]. Adult dogs are most affected at the age of 39 weeks to 56 weeks (Salt *et al.*, 2005; Morris and Dobson, 2001) [23, 15]. Animals under one year of age are at risk in endemic place. The incidence of this disease is higher in female animals than in male animals. This is because the male spreads the TVT by mating with many female animals (Das and Das, 2000) [3]. Although there is no known genetic history of the disease, terrier dogs have been reported to be more susceptible to mammary tumors, ovarian cancer, melanoma and TVT (Gonzalez *et al.*, 2000) [7]. TVT is found outside Reproductive organs and is usually spread by transmission of cells during Coitus (Stockmann *et al.*, 2011) [25]. However, it can also be spread by licking, sniffing, biting, scratching or scratching the affected part of the tumor, or through damaged skin or mucosa (Ozyurtlu *et al.*, 2008; Gulcubuk and Gurel, 2003; Liao *et al.*, 2003; Jonston *et al.*, 2001; Konuk *et al.*, 2001) [19, 8, 12, 9, 11]. After transmission growth of tumor occur between 14th and 60h days, TVT slowly grows or invades over years and eventually becomes malignant and metastatic (Martins *et al.*, 2010; Purohit, 2009) [14, 20]. Vaginal and bleeding discharges are often observed during examination. Other symptoms may include licking outside the vagina and a dangling ball in the area (Ekici, 2015) [5].

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In female dogs, tumors are usually located in the posterior genital area and usually at the vestibulovaginal junction. In male dogs, it is usually found in the tail of the penile region, the gland of the head of the penis or, and the glans penis (Purohit, 2009; Nak *et al.*, 2005) [20, 16]. The localization of the tumor has diagnosis role round cell tumors of the organs should be considered TVT until diagnosed with special techniques such as electron microscopy or immunohistochemistry (Ekici, 2015) [5]. TVT diagnosis is based on physical examination and TVT cytology findings on exfoliated cells obtained by swab, fine needle aspiration, or tumor stamp (Richardson, 1981) [21]. The cells in the smear were determined to be venereal tumor cells, polymorphonuclear leukocytes (PMN), erythrocytes, parabasal cells, intermediate cells, and superficial cells with and without nuclei. TVT positive animals were determined to have more red blood cells and average density than negative animals, and no involvement of other cells was observed, TVT cell negative dogs have more parabasal cells, intermediate cells, and nucleated/nucleated surface cells than positive ones. Therefore, male dogs without lesion can be infected with TVT. To determine the presence of TVT, dogs need to undergo not only a clinical examination but also cytology. This approach may be a simple way to detect and treat dogs with non TVT lesions (Cingi, 2020) [1]. Vincristine sulfate used to treat lymphoproliferative cancers, infectious venereal tumors, thrombocytopenia, and some sarcomas (Sankar *et al.*, 2016; Chun *et al.*, 2001) [24, 2]. At the beginning of the treatment, immediate involution is rapid, but as time, the involution rate slows down and the involution of skin lesions becomes gradual. In general, complete recovery can be achieved with 28 treatments and the treatment success rate is 90%, some side effects are expected. Cytotoxic drugs such as vincristine may cause side effects such as myelosuppression and gastrointestinal disturbances, which may cause leukopenia and vomiting in 5-7% of Dogs (Das and Das, 2000) [3].

Materials and Methods

The study was performed at the clinic and laboratory of registered Manali Strays Trust in Manali Kullu Himachal Pradesh. A total of 40 Himalayan dogs rescued, at the altitude ranges 1900 meters to 3300 meters from sea level. Aged from 1 to 13 years and body weight 8 to 48 kg were evaluated from January 2023 to December 2023. Clinical examination of dogs in normal quadrupedal posture was performed to detect TVT. Abnormal preputial discharge from the genital organ, inflammation of region, redness and tumors growth visible. Collection of samples by using Sterile swabs. Distilled water, ethyl alcohol (96%) and Giemsa staining solution is used for the smear preparation and examination. Compound light microscope is used to cell counts and cell determination. During cell counting, examine the preparation with a light microscope and be careful to count non overlap cells. Microscopic results were cells of TVT, Red blood cells, parabasal intermediate, nuclear superficial or anuclear superficial cells and polymorphonuclear leukocytes PMNs. TVT cells has assessed for nucleocytoplasmic ratio and intracytoplasmic vacuole were transparent luminous. Scoring of cells done based of density low-density, high-density. The smear observation during cytological exam has TVT cells were marked as positive all TVT positive dogs were treated with vincristine sulphate at dose rate of 0.025 mg/kg intravenously diluted with normal saline once weekly along with pantoprazole at dose rate of 1mg/kg intravenously

administered to prevent from gastrointestinal disorder or gastritis, vomiting and anorexia.

Results and Discussion

Clinical improvement was seen from the first week of chemotherapy. Overall tumor shape and size drastically reduced along with bleeding from external genitalia is reduced or stopped, licking of organ, reduction in tumour ulceration. Total 37/40 (92.55%) were TVT positive among these 18 males (90%) and 19 females (95%) were found TVT cells positive in cytological examination. 3 dogs (2 male 1 female) completely cured after administering first dose of vincristine chemotherapy. 15 dogs (7 male, 8 female) were recovered after second dose if intravenous injection. 12 dogs (7 Male, 8 female) cured after third dose. 4 Dogs (2 Male, 2 female) were completely recovered. After administering fifth dose of vincristine last 3 dogs were not completely cured showed partial response, clinical sign was alleviated. TVT can be effectively analyzed in male dogs based upon nearness of ordinary TVT cells watched by cytologic examination after the collection of penis/preputial smear tests from the fauna (Erünal Maral *et al.*, 2000) [6]. It was detailed that the breed, age and sex of the dogs was not of centrality in these periods when all dogs may be similar to transmission. (Das and Das 2000) [3]. Based on cytologic examinations, the number of male dogs that did not have any clinical TVT lesions but had TVT cells was 13 (8.97%) Ortega-Pacheco *et al.* 2006) [17]. Complete response of TVT, 34/37 Dogs (91.89%) were cured and completed alleviation of clinical signs were occur from the seven day after the first chemo dose of vincristine. Three dogs were showing partial response after injecting 4 doses of Inj. Vincristine. (Tella *et al.* 2004) [26] Witnessed complete response of TVT within 35 days, (Martins *et al.* 2008) [13] also did similar treatment and found gradual tumor response although the response was noticeable and significant at the beginning of treatment which regressed gradually later. (Nak *et al.* 2005) [16] Found similar results with complete response of TVT in 31 of 37 dogs after 2-7 dose of vincristine. Treatment with Inj. Vincristine @ 0.025 mg/kg i/v at weekly intervals for five weeks with which complete remission was achieved in 75 dogs with a median of 5 Injections. (Said *et al.* 2009) [22]. TVT Cells informs that the dogs infected with TVT cells and therefore, the density of the inflammatory cells was increased. These results indicate that response to treatment differs among the individual dogs.

Conclusion

The study reveals that TVT cells can be Seen by using cytology even when no prominent TVT lesions visible, which is important for the analysis of TVT. The results showed that animals with genitals and preputial prepared had TVT cells that could be newly infected. We conclude that these findings alone are not sufficient to diagnose TVT and that regular monitoring of the disease using cytology from genitalia is important, even if TVT lesions are not found. Cytological tests play a key role in diagnosis of TVT in remote areas of high altitude of Himalayas where basic diagnostic facility is not for the animals, TVT control is very difficult in Himalayas because most stray dogs are the carrier and it's difficult to rescue the dogs in mountain terrain. Vincristine sulfate is used to treat the TVT thrombocytopenia, lymphoproliferative cancers, transmissible venereal tumors, other sarcomas. Administration of vincristine sulphate intravenously weekly. It has been proven to be the most effective treatment.

Future scope

Monitoring the dogs carefully in pens and kennels before coitus, prevention of breeding animals, dog license laws, control of potentially infected reserve and preventing roaming of stray animals would help in controlling rate of the disease. Vincristine accuracy will be increase with combination of other drugs. Prevention in feral dogs also preventing another wild canine.

Conflict of Interest

The authors declare that there is no conflict of interest among them. This means that there are no financial, personal, or professional relationships or circumstances that could potentially influence or bias their contributions to this work. The research and its findings are presented impartially and without any competing interests that might impact the objectivity of the study.

Author contributions

Akash Bairwa-collection of data, Rebecca Metacalf-contributed data and analysis tools, perform analysis, wrote the paper.

Shashikant-Conceived and designed the analysis, contributed data and analysis tools, perform analysis.

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