The Pharma Innovation Journal 2023; 12(4): 2700-2702

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277-7695
ISSN (P): 2349-8242
NAAS Rating: 5.23
TPI 2023; 12(4): 2700-2702

www.thepharmajournal.com
Received: 06-02-2023
Accepted: 16-03-2023

A Sabarinathan
Assistant Professor, Department of Veterinary Clinical Complex, Veterinary College and Research Institute, Tamil Nadu Veterinary and Animal Sciences University, Tirunelveli, Tamil Nadu, India

Chhavi Gupta
Assistant Professor, Department of Veterinary Gynaecology and Obstetrics, Veterinary College and Research Institute, Tamil Nadu Veterinary and Animal Sciences University, Tirunelveli, Tamil Nadu, India

A Thangamani
Assistant Professor, Department of Veterinary Gynaecology and Obstetrics, Veterinary College and Research Institute, Tamil Nadu Veterinary and Animal Sciences University, Tirunelveli, Tamil Nadu, India

A Ganesan
Assistant Professor, Department of Veterinary Gynaecology and Obstetrics, Veterinary College and Research Institute, Tamil Nadu Veterinary and Animal Sciences University, Tirunelveli, Tamil Nadu, India

M Balagangatharathilagar
Associate Professor and Head, Veterinary Clinical Complex, Veterinary College and Research Institute, Tamil Nadu Veterinary and Animal Sciences University, Tirunelveli, Tamil Nadu, India

Dr. V Prabaharan
Associate Professor and Head, Department of Veterinary Gynaecology and Obstetrics, Veterinary College and Research Institute, Tamil Nadu Veterinary and Animal Sciences University, Tirunelveli, Tamil Nadu, India

Corresponding Author:
A Sabarinathan
Assistant Professor, Department of Veterinary Clinical Complex, Veterinary College and Research Institute, Tamil Nadu Veterinary and Animal Sciences University, Tirunelveli, Tamil Nadu, India

Analyses of combination chemotherapy effectiveness for canine transmissible venereal tumor in 188 indigenous dogs

A Sabarinathan, Chhavi Gupta, A Thangamani, A Ganesan, M Balagangatharathilagar and Dr. V Prabaharan

Abstract
Canine transmissible venereal tumor occurs in sexually active dogs of tropical and subtropical region. The tumor is of near constant karyotypic variation of 58-59 chromosomes against the normal chromosomes number of 78 in dogs. Southern district of Tamil Nadu state is well known for the pure germplasm of indigenous dog breeds namely, Chippiparai, Kanni, Rajapalayam and Kombai such indigenous breeds were more prone for the Canine Transmissible Venereal Tumor (CTVT). The study was carried out in 188 indigenous dogs confirmed with CTVT. In Group I 94 dogs were treated with Inj. Vincristine sulfate @ 0.025 mg per kg b.wt via Intravenous (IV) route at 7 days interval 4-8 doses. In group II 94 dogs were treated with Inj. Vincristine sulfate @ 0.025 mg per kg b.wt via Intravenous (IV) route along with Inj. Ivermectin @ 200 mcg per kg b.wt subcutaneous (SC) at 7 days interval 4-6 doses.

Keywords: CTVT, impression smear, vincristine sulfate, ivermectin

Introduction
Canine transmissible venereal tumor is abnormal tissue growth with no purposeful function, and is characterized by independent and unrestrained growth. Phylogenetic analyses indicate that canine transmissible venereal tumor (CTVT) most likely originated from a wolf or an East Asian breed of dog between 200 and 2500 years ago. CTVT is mostly observed in free-roaming, sexually active dogs in tropical and subtropical regions such as the southern US, Central and South America, southeast Europe, Ireland, Japan, and China (Eze *et al*., 2007) [1]. CTVT is usually transmitted among dogs through sexual intercourse but may also spread through licking, biting, and sniffing tumor-affected areas (Das and Das, 2000) [2]. CTVT is a contagious venereal tumor found in the domestic dog and other social canids that is naturally transmitted between dogs by the allogeneic transfer of living cancer cells during coitus. CTVT cause discomfort, ache, serosanguineus and hemorrhagic discharge noticed from cauliflower like or discrete pin head sized mass. The dogs with active reproductive age and free-ranging were most susceptible and prone to CTVT.

Materials and Methods
A total of 188 dogs comprises of male and female brought to the Veterinary Clinical Complex, Veterinary College and Research Institute, Tirunelveli of Tamil Nadu Veterinary and Animal Sciences University was included in the study. Male and female dogs brought with history of serosanguineus discharge, swollen perineal region (Fig.1), protruding reddish mass from external genitalia and frequent licking of vulvar area and preputial orifice in female and male respectively and were subjected to general clinical examination followed by reproductive examination. All the dogs were subjected to the CTVT screening by means impression smear and vaginal exfoliative cytology method based on the location of tumor mass and the samples subjected to the field staining protocol and examined under microscope, samples with round cells, eccentrically placed nucleus and cytoplasmic vacuoles were confirmed as a case of CTVT. A total of 188 confirmed cases of CTVT included for this study. In Group I 94 dogs comprises of 33 males and 61 females underwent Inj. Vincristine sulfate @ 0.025 mg per kg b.wt via Intravenous (IV) route at 7 days interval 4-8 doses. In Group II 94 dogs comprises of 28 males and 66 females underwent Inj. Vincristine sulfate @ 0.025 mg per kg b.wt via Intravenous (IV) route at 7 days interval 4-6 doses along with Inj. Ivermectin @ 200 mcg per kg b.wt subcutaneous (SC) at 7 days interval 4-6 doses.

Results and Discussion

In Group I out of 94 dogs received Inj. Vincristine sulfate @ 0.025 mg per kg b.wt via Intravenous (IV) route at 7 days interval 4-8 doses 70 dogs recovered from the transmissible venereal tumor. CTVT recurrence was observed after 6 months from the last dose of chemotherapy in 18 dogs out of 70 dogs responded to the chemotherapy. The treatment success rate and tumor recurrence rate of dogs subjected to group one were 74.46 and 25.10 percent, respectively.

In Group II out of 94 dogs treated 81 dogs fully recovered within 4 to 6 weeks of chemotherapy along with parenteral route of ivermectin therapy. CTVT recurrence was observed after 6 months from the last dose of chemotherapy in 5 dogs out of 81 dogs responded to the chemotherapy (Fig.5). Also, in five of the cured dogs, the cancerous tumor recurred six months later. The treatment success rate and tumor recurrence rate of dogs subjected to group two were 86.17 and 05.30 percent respectively.

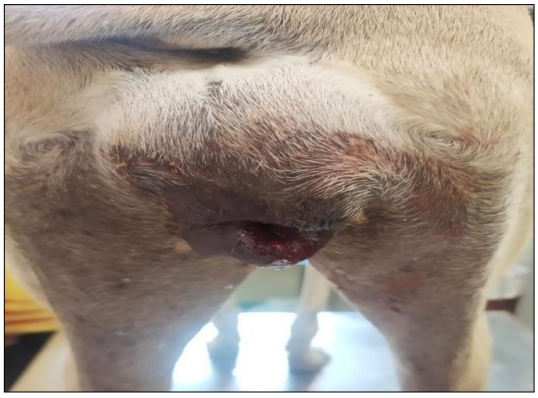

Fig 1: Swollen perineal region in dog with TVT

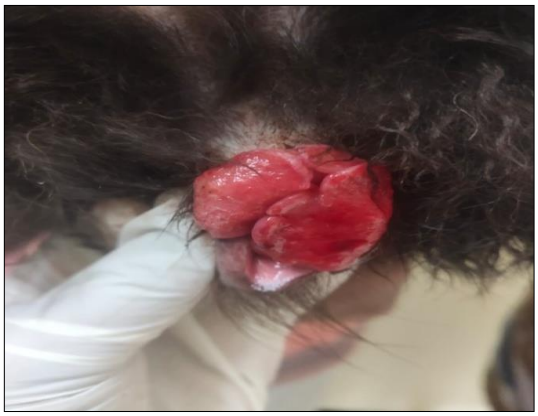

Fig 2: Protruding ulcerated mass on the external genitalia

The majority of CTVT cases received was brought with the history of serosanguines vaginal and preputial discharge, protruding ulcerated mass on the external genitalia (Fig.2), excessive licking of genital area as described by Nak *et al.* (2005) [3] and in few cases bitches brought for breeding advice and stud males brought for breeding soundness examination/semen analysis was confirmed as a case of CTVT. There are variations among the individual dogs noticed for the location of tumor mass namely vulvo-vestibular junction, posterior vaginal wall, floor, roof and dorsal, ventral commissure of vulval lips in bithces similar findings were reported by Madewell (2001) [4]. In males the common locations of tumor mass observed are around the bulbus glandis (Fig.3), pars longa glandis glans penis and preputial cavity and similar findings were reported by C.M. Boscos (2004) [6]. Based on the cytology (Impression smear) definitive diagnosis was arrived following the detailed observation of smear stained with field staining method. On the basis of cytological characteristics such as round cells morphology, scarce cytoplasm, presence of cytoplasmic vacuoles (Fig.4), round nucleus placed with rough chromatin and similar findings were reported by Amaral *et al* (2007) [6]. CTVT shows higher resistance to the antitumoral action of vincristine sulfate (Gaspar *et al*., 2010) [7]. Korystov *et al* (2004) [8] demonstrated the synergistic effect of a combination of avermectin and vincristine that may increase the antitumor effect of the antineoplastic agent and reduce resistance to vincristine.

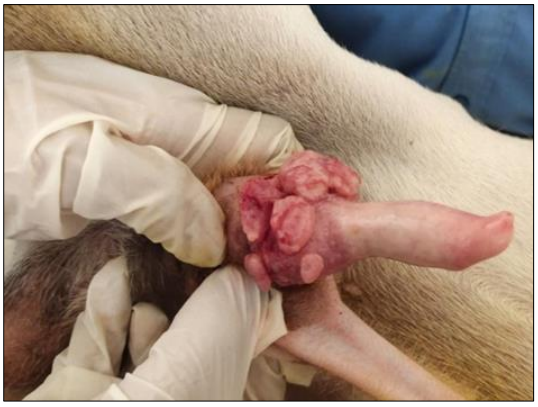

Fig 3: Tumor mass around the Bulbus Glandis

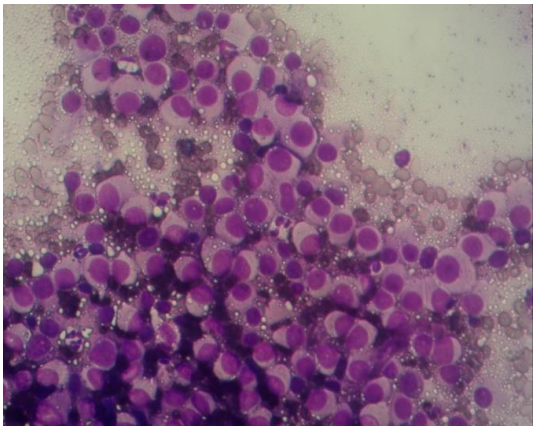

Fig 4: TVT cells with cytoplasmic vacuoles

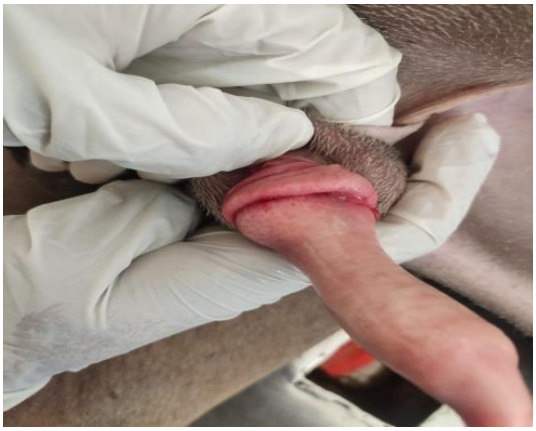

Fig 5: Complete regression of tumor mass after chemotherapy

The superior efficacy of combination of vincristine sulfate and parenteral ivermectin chemotherapy regimen might be due to the synergistic effect of ivermectin which as powerful antitumor activity through the inhibition of proliferation, metastasis, and angiogenic activity and promotes programmed cancer cell death, apoptosis, autophagy and pyroptosis in a variety of cancer cells. Ivermectin can also inhibit tumor stem cells and reverse multidrug resistance and exerts the optimal effect when used in combination with other chemotherapy drugs as described by Mingyang *et al.* (2021) [9]. The present study also revealed that the recurrence of CTVT apart from drug resistance there are recurrence cases we received due to retransplantation of new set of tumor cells after complete recovery if the animal is again exposed to canids with transmissible venereal tumor in subsequent breeding cycle.

Conclusion

The present study showed that the combination of vincristine sulfate and parenteral ivermectin therapy found to be efficacious method of chemotherapeutic regimen for CTVT interms of tumor regression, cure rate with shorter duration of chemotherapy and fewer recurrence rates.

Acknowledgement

The authors are thankful to Veterinary Gynaecology and Obstetrics Unit, Veterinary Clinical Complex, Veterinary College and Research Institute, Tirunelveli and Director of Clinics, Tamil Nadu Veterinary and Animal Sciences University for providing facilities to conduct the study.

References

1. Eze C, Anyanwu H, Kene R. Review of canine transmissible venereal tumor (TVT) in dogs. Nigerian Vet J. 2007;28:54-70.
2. Das U, Das AK. Review of canine transmissible venereal sarcoma. Vet Res Commun. 2000;24:545-556.
3. Nak D, Nak Y, Cangul I, Tuna B. A clinic pathological study on the effect of vin-cristine on transmissible venereal tumor in the dogs. J Vet Med A Physiol Pathol Clin Med. 2005;52(7):366-70.
4. Madewell R. Cellular proliferation in tumors: a review of methods, interpretation, and clinical applications. J Vet Intern Med. 2001;15(4):334-40.
5. Boscos CM. Canine TVT Clinical Findings, Diagnosis and Treatment. Proceedings of World Small Animal Veterinary Association World Congress; c2004.
6. Amaral AS, Silva S, Ferreira I, Fonseca LS, Andrade FH, Gaspar LFJ. Cytomorphological characterization of transmissible canine venereal tumor. Rev Port Cien Vet. 2007;102(563-564):253-260.
7. Gaspar LFJ, Ferreira I, Colodel MM, Brandao CVS, Rocha NS. Spontaneous canine transmissible venereal tumor: cell morphology and influence on P glycoprotein expression. Turk. J Vet. Anim. Sci. 2010;34(3):447-454.
8. Korystov YN, Krmakova NV, Kublik N, Levitman MK, Shaposhnikova VV, Mosin VA, *et al*. Avermectins inhibit multidrug resistance of tumor cells. European Journal of Pharmacology. 2004;493:57-64.
9. Mingyang T, Xiaodong H, Wang Y, Xin Y, Zhang W, Chenying Y, *et al*. Ivermectin a potential anticancer drug derived from an antiparasitic drug. Pharmacol Res. 2021;163:105207.