Short Communication

A NOVEL THERAPEUTIC COMBINATION OF VINCRISTINE AND IVERMECTIN IN THE TREATMENT OF TRANSMISSIBLE VENEREAL TUMOUR IN BITCHES

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ABSTRACT

The transmissible venereal tumour (TVT) is a contagious neoplasm that is sexually transmitted between dogs. TVT lesions affect the mucus membranes of the external genitalia in dogs of both sexes. Tumour masses are seen in the caudal aspect of the penis and frequently the prepuce area in males and the posterior vaginal area, particularly the vestibule vaginal junction of females. Sixteen bitches of various ages (2-6 years) and breeds were brought to the clinics at Veterinary Clinical Complex, Gannavaram with the history of continuous oozing of blood from vagina, anorexia and depression. All these were diagnosed as TVT based on the history, clinical symptoms and cytological examination and therapy was initiated. At weekly intervals, all the bitches were administered with combination therapy of Vincristine sulphate (0.025 mg/kg body weight, strict and slow I/V) and Ivermectin (0.2 mg/kg body weight, strict S/C) for four consecutive weeks. All of the bitches underwent significant reduction in tumour size with improvement in general health during the course of therapy with exception that one bitch showed signs of anorexia and dullness.

Keywords: Ivermectin, Transmissible venereal tumour, Treatment, Vincristine

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Transmissible venereal tumour (TVT) or venereal sarcoma is a horizontally transmitted tumour that spreads from one animal to other animal by transfer of viable neoplastic cells during copulation in dogs (Abeka, 2019). It mainly affects the external genital organs and rarely the interior genital organs. Due to its unique immunological features associated with transmission and spontaneous regression in the natural host, TVT has recently been explored as a model for understanding neoplastic disorders (Frampton *et al.,* 2018). The treatment of choice for TVT is vincristine sulphate (Scarpelli *et al.,* 2010), which is administered at weekly intervals

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until tumour remission; however, vincristine therapy can result in adverse reactions affecting bone marrow and gastrointestinal tract (Ramadinha *et al.,* 2016).

Drug resistance is the primary disadvantage of vincristine therapy in the treatment of TVT cases. Ivermectin, on the other hand, can reverse antineoplastic medication resistance by inhibiting p-Glycoprotein (P-gp) production within the tumor cells (Jiang *et al.,* 2019). Recent research also suggests that ivermectin could be employed as an anticancer medication (Jiang *et al.,* 2019). Very recently it has been suggested that novel alternatives are needed to combat the consequences of drug resistance associated with vincristine therapy (Sewoyo and Kardena, 2022).

Sixteen bitches of different breeds and ages (2-6 years) were brought to the clinics at Veterinary Clinical Complex, Gannavaram with a history of continuous sanguineous vaginal discharge from vagina, anorexia and depression. On vaginal examination, cauliflower-like pedunculated growth with ulcerated surfaces were noticed. Field's stain A and B were used to stain the impression smears taken from the pedunculated masses, which revealed round to oval shaped cells with intracytoplasmic vacuoles and a single conspicuous nucleus (Fig. 1). Based on history, clinical signs and cytological examination, all of the cases were diagnosed as TVT and treatment was initiated. For four consecutive weeks, all the bitches were administered with Vincristine sulphate (0.025 mg/kg b.wt, strict and slow I/V) and Ivermectin (0.2 mg/kg b.wt, strict S/C) at weekly intervals. During the course of treatment, the size of the pedunculated tumour masses in the treated bitches diminished significantly (Fig 2a-2d); nonetheless, one bitch had experienced side effects such as anorexia and dullness.

TVT is an immunogenic tumour, and the host immune system plays a critical role in the development of TVT, with the disease outbreak indicating the neoplasia's ability to overcome the host immune system (Kumar *et al.,* 2021). The tumor's anatomical location and cytology are used to make the diagnosis. TVT's are composed of homogeneous tissue with compact cellular mass produced from mesenchymal tissue. The findings of the present case report indicated that combination of vincristine sulphate and ivermectin therapy was the most effective chemotherapeutic agent for treating TVT in dogs (Filho *et al.,* 2020). It acted by preventing mitosis at the metaphase stage of cell division (Said and Tsimberidou, 2014). However, according to a study, drug resistance due to vincristine therapy was caused by the over expression of a protein molecule termed P glycoprotein from the tumour cell (Gaspar *et al.,* 2011). Bulhosa *et al.* (2020) used a combination therapy that included vincristine sulphate and ivermectin to combat drug resistance associated with vincristine. They concluded that ivermectin functions as a substrate for P-glycoprotein, reducing its expression in tumour cells and thereby preventing drug resistance caused by vincristine. Similarly, the present case study revealed improved tumour regression, general animal health and animal comfort throughout the course of treatment in all the bitches. To summarize, the present case report demonstrated that the combination

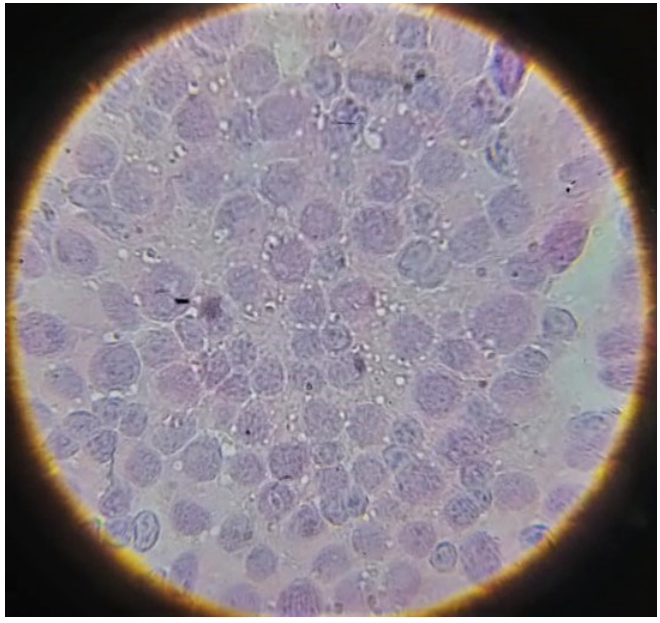

Fig. 1. Round to oval shaped neoplastic cells with intracytoplasmic vacuoles in the impression smears. Fields's stain; x 40

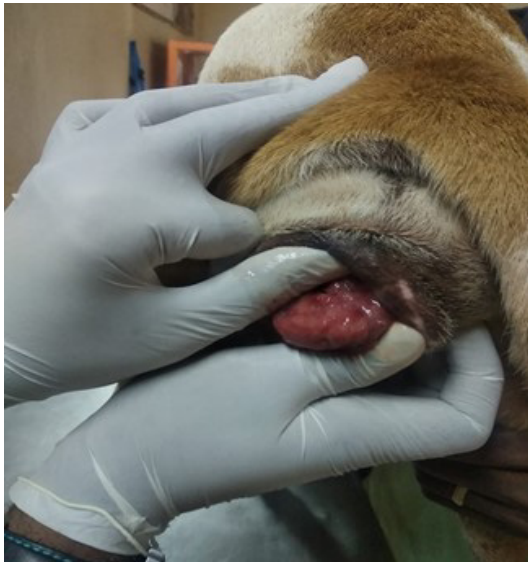

Fig. 2a. Tumor mass after 1st dose of treatment

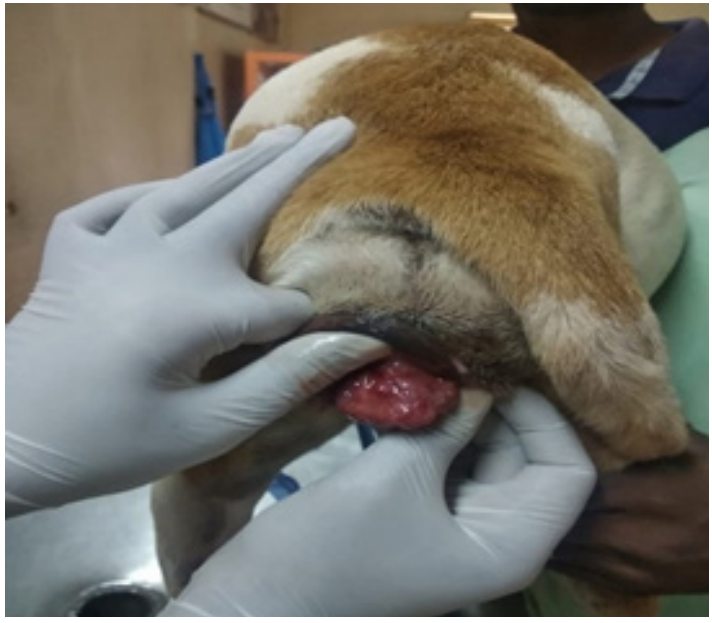

Fig. 2b. Tumor mass after 2nd dose of treatment

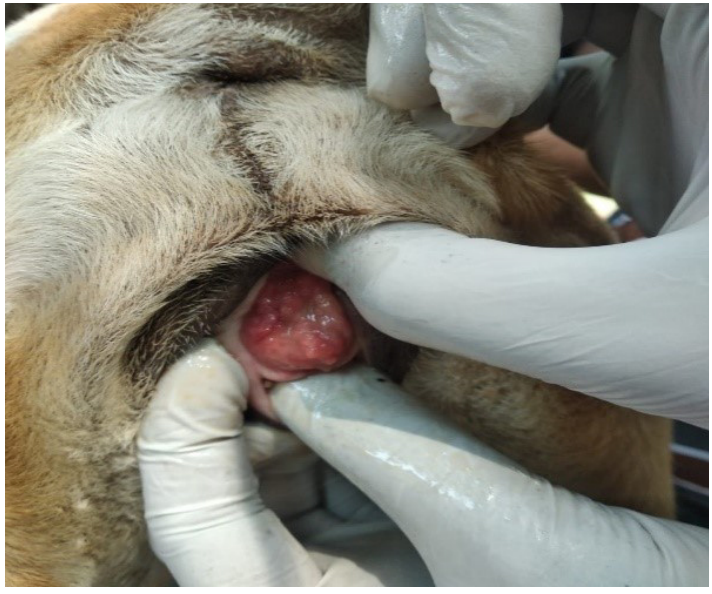

Fig. 2c. Tumor mass after 3rddose of treatment

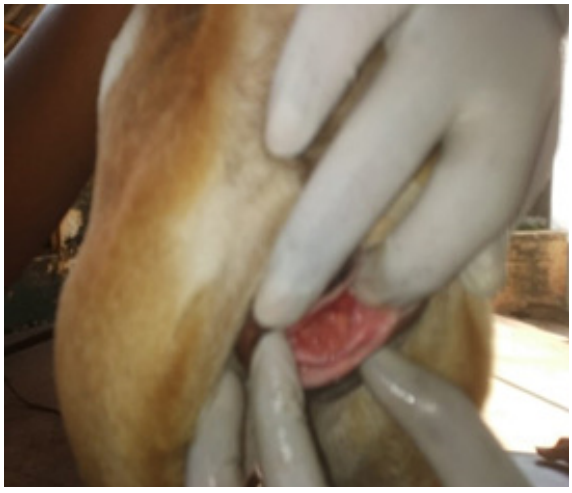

Fig. 2d. Tumor mass after treatment

of vincristine sulphate and ivermectin for the treatment of TVT was found effective and well tolerated as evinced by very few adverse effects in the treated dogs. Nonetheless, because there have been few reports of this drug combination and its utilization, more research is needed to successfully deploy it.

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