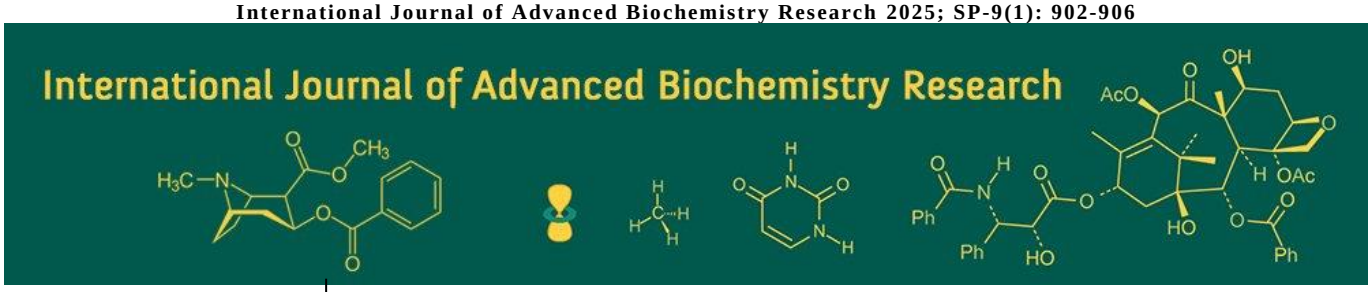

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Histopathological alteration in venereal transmissible tumour affected female dogs using chemotherapy

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Abstract
Canine Transmissible Venereal Tumor (CTVT) is a histiocytic tumor primarily affecting the external genitalia of dogs transmitted through copulation. It is typically localized to the genital area and rarely metastasizes. The present study was conducted on 30 female dogs that were presented for complaint of growth in vagina with bleeding in T.V.C.C, Mhow. The twelve female dogs out of thirty were categorized as chemotherapy by vincristine sulphate and cyclophosphamide. The biopsy samples of tumorous growth were collected for on the day before chemotherapy and after one week of chemotherapy or till regression for histopathological evaluation. Before chemotherapy most of the cells were in compact masses or sheet as cords, or loose in a delicate stroma**.** Regressing size of neoplasm demonstrated a decrease in number of tumour cells and their eventual disappearance along with oedema, haemorrhage and infiltration of neutrophils. Plasma cells fibrosis developed in the terminal stage of regression. In animals undergone therapy by vincristine sulphate the mean mast cell values at days 0 and 7th got (p<0.01) significantly reduced, however the cyclophosphamide therapy mast cell variations were statistically non-significant.

Keywords: Vincristine sulphate, cyclophosphamide and mast cell

Introduction
Canine Transmissible Venereal Tumor (CTVT) is a histiocytic tumor of dogs and other canids that mainly affects the external genitalia and it transmitted from animal to animal during copulation (Park *et al*., 2006) [11]. It is usually located at the genitalia of both sexes and is rarely found elsewhere in the body, while it metastasizes in only a very few cases. Cotchin (1956) described it as an epithelial tumor, infectious or venereal granuloma, lymphosarcoma or histiocytoma. Several nomenclatures for describing canine TVT were adopted from time to time by different workers. The tumor can be transplanted as an allograft across major histocompatibility (MHC) barriers within the same species, also to other members of the canine family, such as foxes and wolves (Abeka, 2019) [1].
The management of CTVT has not been very easy in dogs, especially in developing countries, as most owners cannot afford the cost of surgical intervention and or radiotherapy. Anticancer drugs like Vincristine sulphate have been described as an effective drug is the salt of an alkaloid obtained from the common periwinkle (*Vincarosa livia*). It has a wider application in human medicine in combined chemotherapy with other anticancer drugs. The surgical excision of CTVT has also been done by a number of scientists with some extent of success but there is an incidence of tumor reoccurrence. Because of the above facts the present study evaluate the histopathological conformation of venereal transmissible tumor before chemotherapy and histopathological changes after chemotherapy.

Materials and Methods
A total of twelve animals were randomly placed in to following 2 groups of 6 animals each to follow different treatment protocols. Group I animals undergone chemotherapy by administration of vincristine sulphate @ 0.025 mg/kg B. wt. and group II using cyclophosphamide @ 10 mg/kg B. wt., intravenously with normal saline at weekly intervals till complete regression of the tumor.

Histopathology

The biopsy samples of growth were collected for histopathological studies on the day before chemotherapy and after one week of chemotherapy or till regression and were fixed in 10% buffered formalin and passed through acetone benzene series and embedded in paraffin. Sections were cut at 5 micron thickness & stained with haematoxylin and eosin (Gridley, 1960) [5].

Special stain using Toluidine Blue and counting of mast cells (Rao, 2004) was done to check the stage of tumour growth and regression of the tumour before and after chemotherapy. The number of mast cells were calculated in 10 active fields under 400 magnifications under light microscope as narrated by Park *et al*. (2006) [11] and Ahuja *et al.* (2011) [2].

Statistical Analysis

Data collected from the study was analyzed, using standard statistical tools as described by Snedeor and Cochran (1996) [13]. The analysis of variance was carried out with the help of two way analysis of variance to see the effect of chemotherapy.

Results

In present study, Cauliflower like tumour growth on external genitalia, bloody discharge and excessive licking of genitalia were the most common clinical signs observed in all the dogs affected with TVT.

The histopathological evaluation of tumour cells before chemotherapy were in compact masses or sheet as cords, or loose in a delicate stroma. The comprising growths stroma was minimal. The cells were uniform except for occasional bizarre cell forms, and were mainly round, ovoid, or polyhedral in outline. They had large, round, hyperchromatic nuclei, distinctly marginal chromatin and large central nucleoli. Further, they had a moderate amount of faintly eosinophilic cytoplasm and the outline of the individual cell was indistinct. Many mitotic figures were found. Lymphocytes, plasma cells and macrophages were scattered irregularly throughout the tumour. Reticular fibers invested small groups of tumour cells in some areas. The neoplastic cells also showed extensive necrosis, since the tumour had an ulcerated surface with hemorrhage and secondary infection.

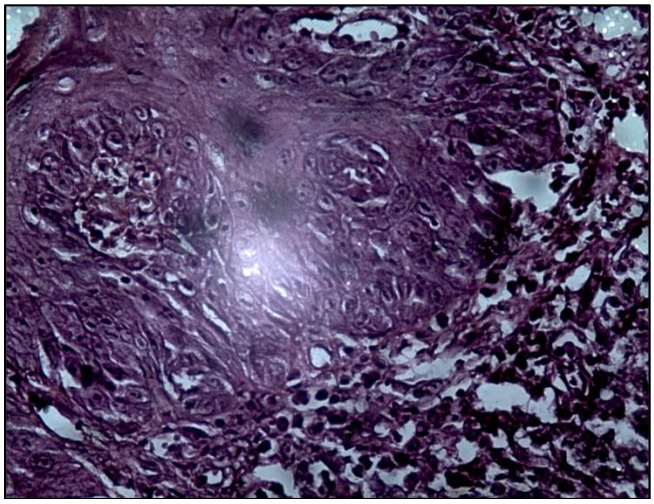

Plate 1: Photomicrograph showing cord formation by tumor cells X 100

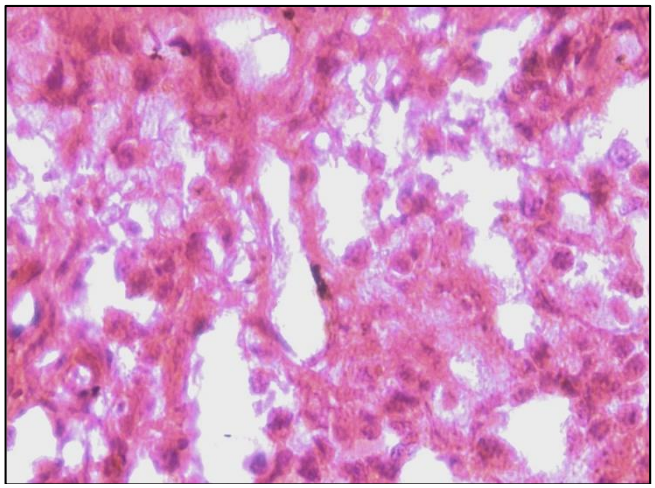

Plate 2: Photomicrograph showing mitotic figure and hyperchromacia X 400

After chemotherapy regressing size of neoplasm demonstrated a decrease in number of dividing tumour cells and their eventual disappearance. Associated with oedema, haemorrhage and infiltration of neutrophils, lymphocytes and plasma cells fibrosis developed in the terminal stage of regression.

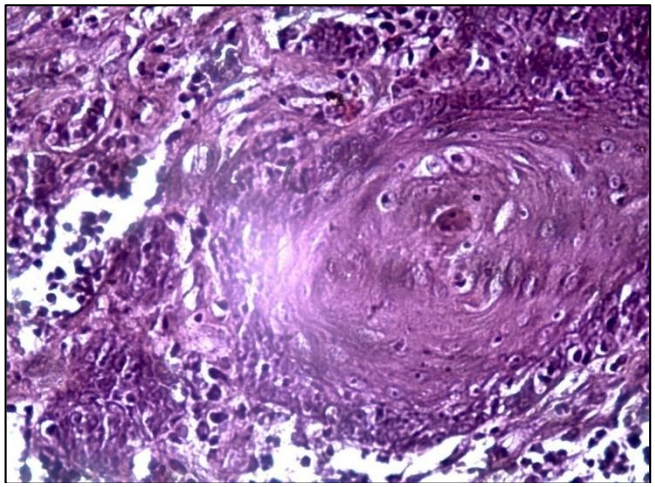

Plate 3: Photomicrograph showing the disappearance of cord formation after vincristine sulphate therapy X 200

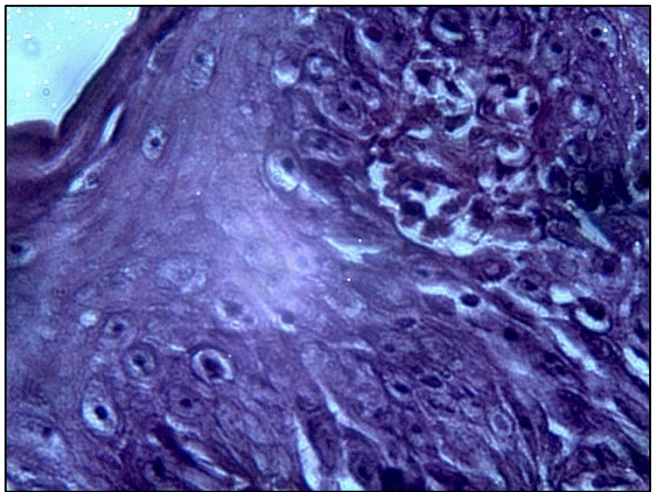

Plate 4: Photomicrograph showing reduction in the tumour cells after vincristine sulphate therapy X 200

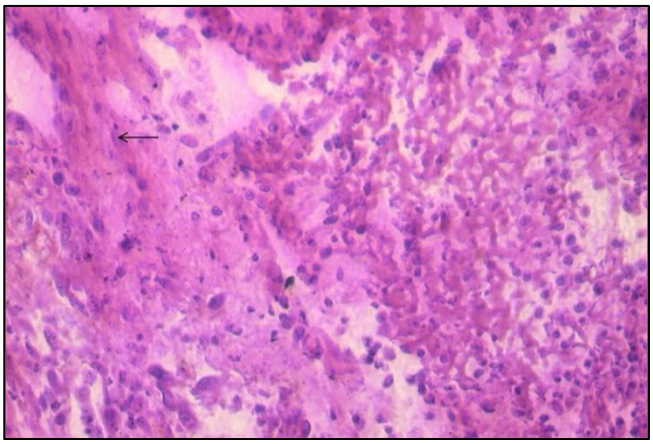

Plate 5: Photomicrograph showing fibrous tissue and regression after cyclophosphamide therapy X 200

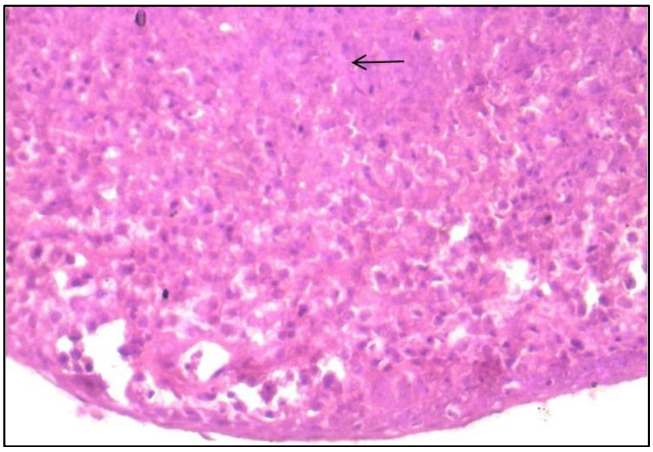

Plate 6: Photomicrograph showing necrosis and regression after cyclophosphamide therapy X 200

Mast Cell count

The animals undergone chemotherapy by vincristine sulphate (group-l) the mean mast cell values in 10 active fields at different periods that is on days 0 and 7th were 52.33±1.96 and 46.17±1.81 respectively. Mast cell counts between periods in this group (p<0.01) got highly significantly reduced.

Table 1: Mean (±SE) Mast cell count (10 active fields) at different time intervals in bitches of group l and group ll.

Group Name	0 day	7th day	t – value
Group 1 (Vincristine)	52.33±1.96	46.17±1.81	4**
Group 2 (Cyclophosphamide)	49.83±1.49	47.83±1.35	1.72^{NS}

** Significant (p<0.01)

A similar trend was noticed in group-ll animals (Chemotherapy by cyclophosphamide) where the mast cell values were 49.83±1.49 on day 0th and 47.83±1.35 on day 7th. However, the variations in these count values were statistically non-significant (Table 01).

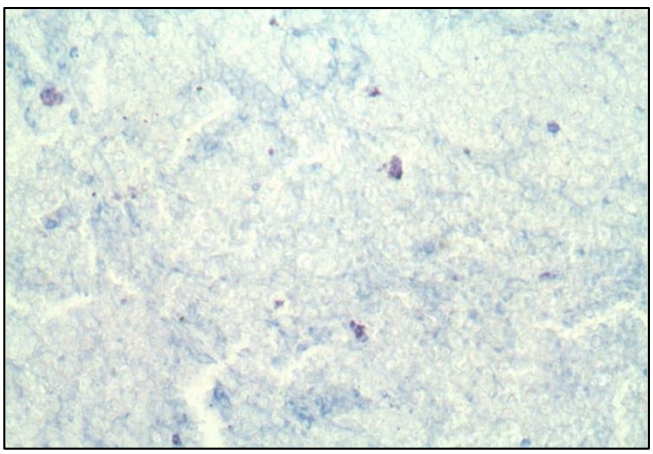

Plate 7: Photograph showing mast cells before chemotherapy X 200

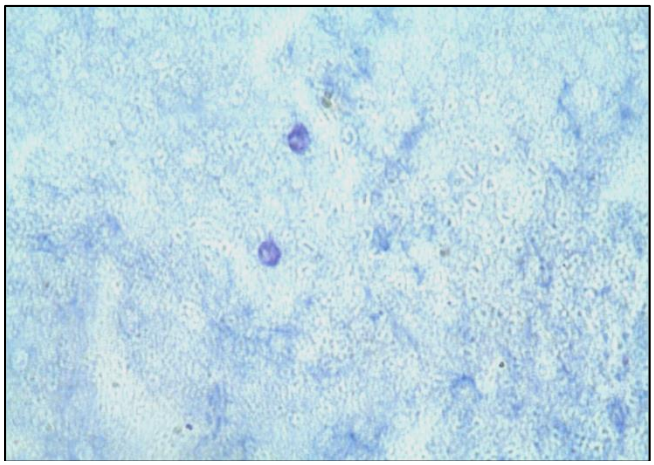

Plate 8: Photograph showing mast cells after vincristine sulphate therapy X 200

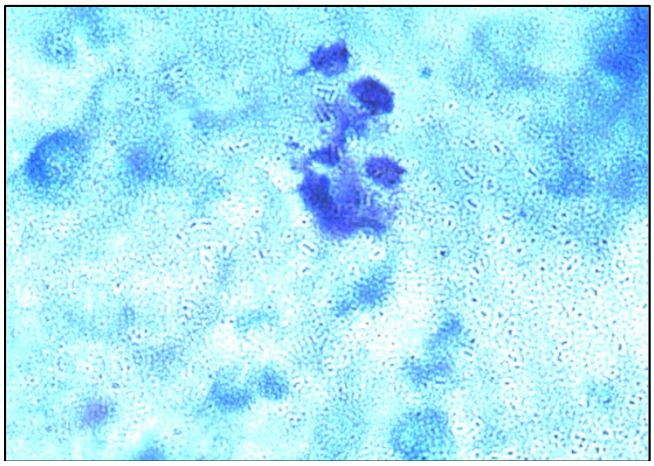

Plate 9: Photograph showing mast cells after cyclophosphamide therapy oil immersion

Discussion

Histopathological examination highlighted round cells in a fibrovascular network, aiding diagnosis (Krithiga *et al*., 2005) [7]. Norris and Withrow (1984) [10] reported that small tumors have larger percentage of cells in proliferating status and cells undergoing rapid division were more susceptible to the effect of anti-neoplastic drugs. Hence tumors that were growing rapidly were most vulnerable to chemotherapy, while slow growing tumors show poor response to chemotherapy, because the percentage of cells that were dividing were fewer.

In most of the groups cells were in compact masses or sheet as cords, or loose in a delicate stroma was minimal. The cells were uniform except for occasional bizarre cell forms, and were mainly round, ovoid, or polyhedral in outline in this study were in accordance with earlier observations (Goldschmidt and Hendrick, 2002) [4]. They had large, round, hyperchromatic nuclei, distinctly marginal chromatin and large central nucleoli. Further, they had a moderate amount of faintly eosinophilic cytoplasm, and the outline of the individual cell was indistinct Jain *et al*., (2002) [6]. Many mitotic figures were found similar with the finding of Thangathurai *et al*., (2008) [14]. Lymphocytes, plasma cells and macrophages were scattered irregularly throughout the tumour (Park, 2006; Yadav *et al*., 2018) [11, 15]. Reticular fibers invested small groups of tumour cells in some areas. The neoplastic cell showed extensive necrosis, since the tumour had an ulcerated surface with hemorrhage and secondary infection (Moulton, 1978) [8].

After chemotherapy decrease in number of dividing tumour cells and their eventual disappearance associated with infiltration of neutrophils, lymphocytes similar finding observed by Jain *et al*., (2002) [6].

The mast cell counts were significantly reduced before and after chemotherapy and a similar trend was noticed by Mukaratirwa *et al*., (2006) [9].

Conclusions

Histopathologically regressing size of neoplasm demonstrated a decrease in number of tumour cells and their eventual disappearance. The disappearance was associated with oedema, haemorrhage and infiltration of neutrophils, lymphocytes and plasma cells. Fibrosis developed in the terminal stage of regression.

Acknowledgments

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