EFFECT OF DOXORUBICIN THERAPY ON TRANSMISSIBLE VENEREAL TUMOUR IN DOGS

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ABSTRACT

The efficacy and toxicity of doxorubicin therapy on transmissible venereal tumors in dogs in comparison with vincristine was studied. Vincristine at the dose rate of 0.025 mg/kg intravenously resulted in complete remission of tumour in five of six cases giving 83.33 per cent success rate while Doxorubicin at a dose rate of 30 mg/m^2 intravenously caused complete remission of tumour mass in five of the six cases (83.33) and partial remission in one. The side effects such as anorexia, vomiting commonly seen with vincristine administration was minimal with doxorubicin hydrochloride.

KEYWORDS: Transmissible venereal tumour, Doxorubicin, Vincristine, Chemotherapy, Dogs

Transmissible Venereal Tumour (TVT) also known as Infectious Sarcoma, Venereal Granuloma, Transmissible Lymphosarcoma or Sticker tumour, is a sexually transmitted benign reticulo endothelial tumour of the dog that mainly affects the external genitalia of young and sexually matured animals. Vincristine sulfate has long been demonstrated to be effective as a single chemotherapeutic agent in the management of canine TVT. However, in the recent years, one drug that has found to play a major role in the improvement of chemotherapy is the anthracycline antibiotics which include Doxorubicin hydrochloride. The present work was undertaken to study the efficacy and toxicity of doxorubicin therapy on transmissible venereal tumors in dogs in comparison with vincristine.

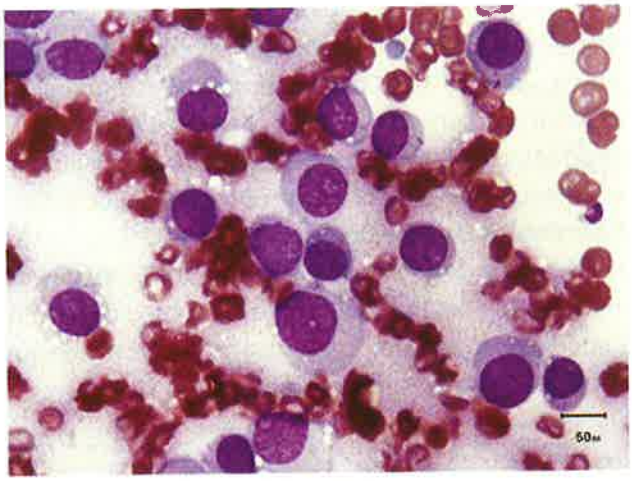

Figure 1
Transmissible venereal tumour cells. Note the nuclear pleomorphism, chromatin condensation and

Twelve dogs of different breeds of either sex aged between 2 and 6 years brought to the small animal gynaecology and obstetrics ward of Madras Veterinary College Teaching Hospital with complaint of bloody discharge and evincing growth in the external genitalia formed the experimental animals for the study. Diagnosis of TVT was made on the basis of clinical signs that included hemorrhagic discharge from the vulva and penis, a visible mass within the prepuce or vulva and abnormal odour. Exfoliative cytology was done to confirm the diagnosis which demonstrated discrete

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cells that were round to oval, with moderately abundant pale blue cytoplasm, an eccentrically located nucleus, with occasional binucleation and mitotic figures (Fig.1). Single or multiple nucleoli were often observed. The most characteristic feature of TVT cells was the presence of numerous discrete clear cytoplasmic vacuoles.

These twelve dogs with TVT were randomly divided into two groups of 6 each. Group I (n=6) dogs were administered with Vincristine (Cytocristin, Cipla pharmaceutical) at the dose rate of 0.025 mg/kg intravenously in equal quantity of saline solution at scheduled intervals of day 0,10, 20 and 30. Group II (n=6) dogs were administered with Doxorubicin at 30 mg/m^2 (Zodox, Intas pharmaceuticals, 50 mg / vial diluted with 25 ml of distilled water) intravenously in 150 ml of normal saline at scheduled intervals of day 0, 10, 20 and 30.

Dogs of both groups were monitored for vital parameters like rectal temperature, heart rate, pulse rate, respiratory rate, behavioural changes and side effects if any during the course of treatment.
Blood samples collected prior to and after each injection were studied to monitor changes in total RBC, WBC, differential count, hemoglobin, SGOT, SGPT, glucose, blood urea nitrogen and serum creatinine. The treatment response in both the groups was evaluated based on inspection of tumour mass and were classified as complete (100%) or partial response.

In the present study, vincristine at the dose rate of 0.025 mg/kg intravenously resulted in complete remission of tumour in five of six cases (83.33 %). In all five dogs the beginning of remission was evident, following the first injection of vincristine itself with visible reduction in the quantity of discharge and size of the tumour mass. One dog that failed to respond to vincristine was subsequently treated with doxorubicin.

In group II dogs, doxorubicin administration caused complete remission of tumour mass in five of the six cases (83.33%) and partial remission in one. Unlike the vincristine group, remission of tumour following doxorubicin therapy was evident only following the 2nd injection. One dog from group I dog that failed to respond to vincristine therapy showed regression of tumour mass when subsequently treated with two doses of doxorubicin. Richardson (1981) and Rogers (1997) have also reported the use of doxorubicin for treatment of TVT cases that were resistant to vincristine therapy.

In group I dogs, side effects such as vomiting, anorexia, alopecia and dullness were commonly observed while in group II, only one dog showed symptoms of alopecia and anorexia while the 7th dog from vincristine group that was subsequently treated with doxorubicin also showed vomiting and anorexia. The anorexia reported was the result of anorexigenic peptides and other intermediary metabolites produced by the neoplasm and the tumour bearing host (Theilen and Madewell, 1987). Vomiting was associated with chemotherapy which usually is the result of either gastric epithelial cell damage or damage to the intestinal epithelial cell surfaces or a stimulation of intestinal afferent input to the vomiting center in the floor of the 4th ventricle (Morrison, 2002). Alopecia probably occurred due to dermatological toxicity while dullness was related due to anemia and severe dehydration.

Although fluctuations in vital parameters such as temperature, heart rate, pulse rate and respiratory rate were observed both within groups and between groups, these changes were within the normal physiological ranges reported for dogs.

No significant changes in the mean RBC values, haemoglobin and eosinophil were observed between treatment days in both groups. A highly significant ($P< 0.1$) decline in mean WBC count from values of 15.79 ± 0.47 on day 0 to 7.2 ± 0.35 x 10^3/µl on day 20 was observed in group I dogs. However, this decline was well within the normal physiological range reported for dogs. Similar decline in WBC values but below the normal physiological range from 13.67 ± 0.60 on day 0 to 5.45 ± 0.42 x 10^3/µl on day 20 was observed in group II dogs. However, in both groups the decline was only transient with levels reaching normal values by day 30. Todorova *et al.* (2005) reported a dose dependent

reversible leukopenia as the predominant manifestation of doxorubicin bone marrow / haematologic toxicity.

The mean neutrophil values in group I dogs significantly declined (pd"0.01) from 3.08 ± 0.13 and 3.11 ± 0.08 x 10^3/µl on treatment day 0 and10 to levels of 2.75 ± 0.20 x 10^3/µl on day 20 which further declined to 2.41± 0.19 x 10^3/µl on day 30 . However, no significant difference in the mean neutrophil count was observed between day 20 and 30. In group II dogs doxorubicin administration caused a significant decline (pd"0.01) in neutrophil count from 3.08 ± 0.91 x10^3/µl on day 0 to 2.53 ± 0.21 on day 10, 0.88 ± 0.20 on day 20 which then significantly increased to 2.50 ± 0.12 x10^3/µl on day 30 respectively. The significantly reversible leukopenia and neutropenia observed following chemotherapy in the present study was probably due to the action of cytotoxic drugs which suppressed the replicating precursor cells of bone marrow and created myeloid toxicity (Todorova *et al.,* 2005).

No significant difference in mean glucose level, blood urea nitrogen, creatinine were observed between treatment days in both the groups. The mean SGOT(IU/L) levels in group I and group II dogs on treatment days 0,10,20 and 30 are 32.81 ± 1.24,39.65 ± 1.07,51.16 ± 0.78 and 59.48 ± 0.64; and 43.50 ± 0.0.61, 47.83 ± 0.94,50.83 ± 0.01and 60.33 ± 0.66 IU/L, respectively. The mean SGOT levels were found to be significantly elevated (pd"0.01) following chemotherapy in both groups. The mean SGPT levels in group I and II dogs on treatment days 0,10, 20 and30 are 20.01±1.36,32.56 ± 1.62,41.85 ± 2.15 and 51.13 ± 1.37; and 32.75 ± 1.59,37.11 ± 1.85,44.43 ± 1.49 and 48.48 ± 2.32 IU/L, respectively. The SGPT levels significantly increased (pd"0.01) throughout the treatment period in both the groups. The increase in SGOT and SGPT levels following chemotherapy in both groups is probably the result of detoxification of vincristine and doxorubicin in the liver (Todorova *et al.*, 2005).

Thus, from the present study it could be concluded that Doxorubicin hydrochloride at the dose rate of 30 mg/m^2 once weekly for four consecutive weeks was found to be effective in treatment of transmissible venereal tumour in dogs with complete remission of the tumour mass in 5 of 6 cases and partial remission in one case.

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