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Research Paper

Transmissible Venereal Granuloma Invasiveness and Response to Chemotherapeutics in Canine

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Abstract

The main aim of this study is to compare the chemotherapeutic effect of vincristine sulfate hydrogel scaffolds and cisplatin hydrogel scaffolds on canine transmissible venereal granuloma. The safety and anti-cancer properties of the scaffold were evaluated by various clinical and biochemical blood parameters before and after treatment of canine transmissible tumor (CTVT). The 12 dogs with canine infectious tumors used in this study were divided into two groups, regardless of gender. A and B. Animals in groups A and B received 0.025 mg/kg vincristine sulfate stent injection and 2.14 mg/kg cisplatin scaffold intravenously per week for four weeks and were repeated 21 days later. To evaluate the response to chemotherapeutic drugs, physical appearance, histopathological changes and blood biochemical parameters related to oncolytic effect were examined at week zero, first, second, third and fourth using standard procedures. Based on the limitations of this study, it was determined that the level of apoptosis was higher in the CTVT cells in the first and second week of the animals applied to the vincristine sulfate scaffold compared to the cisplatin scaffold, according to the symptoms and histopathological examination. Vincristine sulfate hydrogel scaffold was more effective due to tumor regeneration compared to cisplatin hydrogel scaffold.

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1. INTRODUCTION

Cancer can be defined as a disease in which an abnormal cell population grows out of control, regardless of normal cell division. Canine transmissible venereal disease (CTVT) is a disease of dogs and other canines that usually affects the external genitalia and is transmitted through sexual intercourse between animals, but it can also be transmitted through dog bites, kisses, or licking this area. tumor. CTVT alters negative cells along the major histocompatibility complex (MHC), affecting other members of the same species and even canines during sexual intercourse. In India, TVT is the most common disease in dogs, accounting for 23-43% of all cancers. Uncontrolled sexual behaviour and large numbers of stray dogs appear to be the reason for such a high incidence of TVT. TVT has been treated with a variety of treatments, including surgery, radiation, antibiotics, chemotherapy, and chemotherapy. Surgery is commonly used to treat small localized TVTs, but recurrence rates for larger tumors can be as high as 50% to 68%. Chemotherapy has become a method of treatment using a variety of chemotherapy drugs, including vincristine, doxorubicin, and cisplatin. Vincristine sulfate is used as a chemotherapy agent to treat CTVT in dogs, but the drug has several toxic effects. Cisplatin is particularly effective because it has been shown to prevent cancer in many types of cancer, including ovarian

cancer, prostate cancer, and head and neck cancer. Cisplatin faces significant clinical challenges due to drug resistance and serious side effects. Therefore, good drugs need to be introduced into the body to reduce their toxicity and side effects.

The use of encapsulated antineoplastic drugs has many advantages such as increased drug utilization, better bioavailability, high stability, controlled drug release, extended half-life, organ selectivity or tissue and reduction of total dose. Significant difficulties are encountered in treatment due to drug resistance and serious side effects. Therefore, good drugs should be administered to the body to reduce their toxicity and side effects. In light of the above facts, the main purpose of this study is to compare vincristine sulphate hydrogen scaffold and cisplatin hydrogen stent chemotherapy on transmissible venereal tumors in dogs.

2. MATERIALS AND METHODS

Dogs of different breeds, ages and genders with genital warts were examined at the Veterinary Clinical Teaching Centre, G. B. Pant University of Agriculture and Technology, Pantnagar, Uttarakhand, India. The diagnosis of CTVT was confirmed by oncological examination. The treatment was evaluated in a clinical trial in which dogs were randomly assigned to two groups to receive treatment. Vincristine-treated dogs in group A (A-vincristine sulfate scaffold; n = 6) received injections of vincristine sulfate scaffold at 0.025 mg/kg body weight per week for four consecutive weeks and weekly for four consecutive weeks. Dogs in group B (B-cisplatin stent; n = 6) were administered 2.14 mg/kg cisplatin scaffold intravenously and were treated again 21 days later. Physical and clinical symptoms were observed before and after treatment, that is, at weeks 0, 1, 2, 3 and 4 of treatment. After the experiment, the experimental animals were monitored for two months for any adverse symptoms and tumor recurrence. All procedures for animals used in the study were approved by the Ethics Committee and Animal Care Ethics Committee, the clinical center of CTVT, with a letter of recommendation: IAEC/CVASC/VSR/362/dt.21/12/2018 Research to obtain a therapeutic dose is currently being carried out at the Veterinary Clinical Teaching Centre, G. B. Pant University of Agriculture and Technology, Pantnagar, Uttara hand, India. Growth regression of sexual tumors has been studied in previous experiments on a dog with different dosage regimens of each drug.

Clinical Observations and Laboratory Diagnosis

Clinical Parameters

Physical and clinical symptoms were observed before and after treatment, that is, at weeks 0, 1, 2, 3 and 4 of treatment. After the experiment, the experimental animals were monitored for two months for any adverse symptoms and tumor recurrence.

Response of Onoclytic Drugs

The degree of apoptotic effect of different drugs is determined by observing and assessing the size of the tumor and comparing the regression of tumor size before treatment with its original basal size.

Histopathological Examination

Paraffin embedding technique is used in histopathological studies to determine the nature of the tumor. Tissue samples from different groups were collected in 10% formalin buffer at weeks 0, 1, 2, 3 and 4 of the experiment

Haematoxylin and Eosin Staining

Monitoring normal and cytological changes in VENERAL tumor cells on different treatments. Serial sections 6–8 µm thick were cut from each sample using an automated microtome and stained with hematoxylin and eosin. Observe the slide under the microscope and record the damage.

Haematobiochemical parameters

Blood biochemical parameters were examined at weeks 0, 1, 2, 3 and 4 of treatment. Collect approximately 5 ml of venous blood from the tarsal vein or saphenous vein with a sterile sterile solution and then transfer to a sterile bottle (2 ml) containing anticoagulant heparin and another blood vessel (3 ml) for collection of blood. Different hematological parameters viz. Hemoglobin (Hb), hematocrit (PCV), total erythrocyte count (TEC), total leukocyte count (TLC), and differential leukocyte count (DLC) were analyzed. Check the difference in blood chemistry, including blood total protein, blood albumin, blood glucose, blood urea nitrogen, blood creatinine, blood aspartate aminotransferase (AST), blood alanine aminotransferase (ALT), and serum gamma Glutamyl transpeptidase (GGT).

3. RESULTS AND DISCUSSION

The aim of this study was to generate hydrogen scaffolds and to evaluate the oncolytic effects of vincristine sulfate hydrogen scaffolds and cispartine hydrogen scaffolds on transmissible venereal granulomas in 12 female dogs (divided into two groups). Six animals each in A and B. The oncolytic effects of different oncolytic drugs were based on physical appearance, reactivity, histopathological studies and apoptosis studies.

General appearance of venereal tumors in dogs

The data presented in this study have features similar to TVT: pollen-like nodules of various sizes (0.5-5 cm in diameter) and external ulceration. In males, neoplastic masses usually appear as single, multiple, small to large, sessile or pedunculated soft nodular masses at the base of the penis. In women, the tumor often appears in the form of a single cauliflower and masks the external genital organs. The consistency of the tumor is soft and hard. All tumors have irregular, soft and fragile tissue. In rare cases, the tumor breaks down in nature and the animal becomes cachectic. In male dogs, genital tumors are usually found in the tail of the genital area, from the feet to the pupils or throat, and some occur on the foreskin. These findings are consistent with **Rezae *et al*., 2016**. Tumors in both male and female dogs are red to reddish in color due to their blood volume, and because they are fragile, they bleed easily. Patients affected by CTVT are

often characterized by a foul-smelling, persistent or intermittent serous or bloody discharge, and animals often show a persistent soft spotting habit. Urinary incontinence (anal temperature, urination and defecation) is normal in all animals except in one case where excessive urination occurs due to enlargement of the urine. Current findings regarding the appearance and location of granuloma venereum are also supported by **Goldschmidt and Hendrick (2002); Kissani and Adam (2009)**.

Regression of tumour

In this group A, complete regression of tumor size was observed on vincristine scaffolds (**Fig. b and d**). No tumor recurrence or adverse effects of the vincristine stent were observed in patients affected by CTVT during the study period and within three months of treatment or follow-up. Only a slight regression in tumor size was observed in group B animals throughout the study period and after treatment (**Figure f and h**). After the first injection of the vincristine scaffold into the animals in group A, the VENERAL tumor began to shrink rapidly. During physical examination, a 50% reduction in tumor growth was observed in group A animals after the first week. The broadcast is completed after the second week. No tumor recurrence or adverse effects of the vincristine scaffold were observed in patients affected by CTVT during the study period and within three months of treatment or follow-up. Apoptosis induced by the vincristine sulfate scaffold is associated with caspase-3 and 9. The current finding of apoptosis or regression in CTVT is consistent with the observations of **Decker *et al.* (2015)** reported that the tumor regression observed so far with vincristine treatment may be due to its binding to tubulin, a type of tubulin in the brain that acts as an antibiotic. The spindle then fails to function in mitosis and arrests the cell cycle in metaphase (**Garden, 2010; Ganguly et al., 2016 and Antonov, 2017**). **Sharma *et al.* (2011)** and **Antonov, (2017)** reported that vincristine sulfate at a dose of 0.025 mg/kg body weight 3 to 4 times a week is the most effective, safe and easy treatment and can lead to long life. veneral tumors respond to cisplatin scaffold. The reaction is moderate, the outlook has changed slightly. Tumor size gradually returned to some extent over the study period.

Histopathological Studies

Histopathological studies of **fig 1, 2, 3 & 4** in the third week of Group A showed extensive necrosis of the tumor. Tumor cells are highly vacuolated, nuclei are oval or round, large or small, chromatin is coarsely granular, and intercellular collagen fibers are intertwined. Most of the degeneration in the necrotic area has no nucleus. At high magnification, cytoplasm is abundant, vacuoles are present, and the number of mitoses is low. In many areas, single or a group of tumor cells were necrotic and appeared as irregular areas throughout the tumor (Figure 1). The number of apoptotic cells was higher compared to the week 0 blood sample. Besides apoptotic bodies, the presence of shrunken isolated apoptotic cells with condensed chromatin and fragmented nuclei was also observed. From the third week of the studies, tumors in group A animals gradually healed and showed large amounts of intercellular matrix collagen (Figure 2). In the third week, changes were observed by histopathological staining in group A animals. Histopathological examination of Group B veneral tumors was performed every week and a large area of necrotic tumors was detected. Tumor cells are highly vacuolated; oval or round nuclei, large or small, coarse-grained chromatin and staggered collagen fibers between cells. In the histopathological examination of the animals in the fourth group at the fourth week, it was observed that many tumor cells containing thick and granular nuclei and many vacuoles in the cytoplasm began to degenerate **(Figure 4)**. Histopathological studies have revealed areas of round lesions with borders that are not easily distinguishable. **Trompieri (2009)** reported that venereal tumors in dogs have a heterogeneous population of tightly packed, large, round or oval cells with dense but well-circumscribed cytoplasm. The nuclear chromatin is thin and dispersed, the nucleus is large and oval, and the nucleolus is prominent and in place. There is a marked infiltration of lymphocytes, plasma cells and small amounts of macrophages. Mitosis is also seen. The presence of a rounded base in the dendritic fibrovascular network aids in the histological diagnosis of the tumor. These observations are consistent with the findings of K**rithi**g**a *et* a*l*., 200**5. Significant changes in cellular (heterogeneous cell size) and nuclear morphology (heterogeneous cell size) were also observed. The nuclei of tumor cells are round to oval and in situ. Nuclear pleocytosis is evident in tumor cell nuclei. Nucleoli are basophilic and range from one to three. Nuclear chromatin structure is coarse to reticular. The composition and amount of stroma present in transplanted tumors that degenerate are more distinct than in transplanted TVTs that grow similarly to genital TVTs. **Sethawongsin *et al.* (2017) and Murad *et al.* (2019)** The regressed tumor showed cytoplasmic vacuolation. In some cases, neutrophil infiltration and extensive collagen tissue. After the tumor had completely regressed, a biopsy of the penile or genital epithelium of the tumor site revealed mature tissue with no evidence of tumor cells. The submucosa is filled with newly formed blood vessels and connective tissue.

Hematobiochemical parameters

A non-significant (P>0.05) increase in Hb value was also observed in the animals of group A subjected to administration of vincristine scaffolds throughout the period of study. The Hb value was at peak level at fourth week (11.18±0.43) time interval from its base value (10.24±0.45). However, the value at 0 week was non-significantly (P>0.05) lower than the value at first, second and fourth week. There was no significant difference in the level between second and fourth week. There was a non-significant (P>0.05) increase in Hb level in the animals of group B subjected to administration of cisplatin scaffolds. The Hb level in group B showed a consistent and gradual increasing trend up to fourth week (11.25±0.54) from their base value (11.00± 0.13). It was also observed that Hb at third week (11.15±0.36) was non-significantly (P>0.05) lower than the values recorded at first, second- and fourth-week time intervals. In the animals of group A a non-significant (P<0.05) increase in mean Hb (%) level might be due to improvement of chronic loss of ulcerating

surface of tumour mass.This may be due to improvement in blood loss. **Das and Das (2000)** have also observed non - significant (P>0.05) change in Hb (%) in CTVT dogs treated with vincristine along with the combination of cyclophoshamide (@ 50 mg, orally and methotrexate @ 0.35 mg/kg body wt.). However, **Sharma *et al.* (2011)** have observed a significant (P<0.05) increase in hemoglobin (%) in CTVT dogs treated with vincristine up to 3 weeks of studies.

No significant (P>0.05) change in the PCV level was observed throughout the period of study in the animals of group A subjected to administration of vincristine scaffolds, except a slight increase in its value (42.75±1.58) at 3 week time intervals.There was a gradual and non-significant (P>0.05) increase in PCV level in animals of group B from first to fourth week time intervals. The PCV value at second week (41.50±2.57) was higher (P>0.05) than base value (41.23±2.12) in the animals of group B. The values at first, second, third and fourth week did not vary significantly among the animals of group B. Non-significant increase in group A and decrease in group B subjected to administration of vincristine and cisplatin scaffolds may be due to reduce in toxicity by slow release of drugs through scaffolds in vincristine **(Cunha *et al*., 2017)**.

In the animals of group A subjected to treatment with vincristine scaffolds, the levels of TLC showed a significant (p<0.05) decrease throughout the period of study. The TLC values at second week (8.95±0.28), third week (8.85±0.31) and fourth week (8.62±0.25) were significantly (P<0.05) lower as compared to its base value (9.20±0.35). In the animals of group B subjected to administration of cisplatin scaffolds significant (P< 0.05) decrease in TLC level was observed throughout the period of study from first week to third week and then tends to increase toward mean base value at fourth week. There was a significant (P<0.05) difference in the TLC level between 0, second and third week. Significant (P>0.05) changes in TLC level in animals of groups A and B in the present study may be due to depression of reticuloendothelial system **(Birhan and Chanie, 2015)** along with mild myelosuppression with the use of vincristine sulphate **(Dan *et al*. 2018)**.

No significant (P>0.05) changes in neutrophil counts were observed in animals in groups A and B during the study period. Changes in mean neutrophil values at different time periods increased or decreased very close to the baseline value at week 0. Non-significant (P>0.05) changes in neutrophils were detected in animals in groups A and B during the experimental period, probably due to myelosuppression. However, Das and Das (2000) and Sharma et al (2011) did not find significant changes in neutrophil levels in animals treated for cancer.

A significant (P<0.05) change in mean lymphocyte value was observed throughout the period of experiment in the animals of group A subjected to administration of vincristine scaffolds. In the animals of group A, the lowest (32.50±1.58) and highest (38.70±1.22) mean lymphocyte level was observed at 0- and fourth-week times interval, respectively. A non-significant (P>0.05) lymphocytosis was observed in the animals of group B subjected to administration of cisplatin scaffolds. In group B, the mean lymphocyte value increased up to 4 weeks (33.55±2.90) from their mean base value (29.50±2.35) and then tends to decrease and shifts towards normal. The mean lymphocyte value at first, second, third and fourth week were non-significantly (P>0.05) different from their mean value at 0 day. The present finding of lymphocytosis may be due to myelosuppression and was also observed previously by **Mason *et al.* (2014); Srivastava *et al.* (2014) and Cunha *et al*. (2017)**.

A slight and insignificant (P>0.05) decrease in serum protein was observed in group A and B animals that received vincristine and cisplatin scaffold until the fourth week. In both groups, the lowest level occurred in the fourth week. The decrease in protein in the blood is within physiological limits. Decreased total protein (TP) content indicates that intestinal inflammation after vincristine treatment in dogs may cause a minor impairment in absorption and assimilation. This is mainly because anti-cancer drugs often cause cells to break down rapidly. The same observation was reported by **Dan *et al*., 2018. Varug *et al.* (2012) and Ganguly *et al*. (2016)** also found lower total protein levels in canine granulomas, like other canine tumors, compared to normal dogs. Throughout the experiment, no significant (P>0.05) changes in serum albumin levels were observed in animals in groups A and B given vincristine and cisplatin scaffolds, respectively. In this study, serum albumin levels remained within normal physiological limits at various time points in all animals in both groups. Non-significant changes in albumin levels seen at different times in two animal groups do not indicate harmful effects of vincristine and cisplatin on liver hepatocytes (**Antonov, 2017 and M**urad ***et*** al., 2019). There was no significant (P<0.05) change in glucose concentration in animals in groups A and B. In group A, a slight increase (89.50±8.25) was observed in the middle blood sugar results in the first week, then its significance decreased until the third week. In animals in group B, glucose increased slightly above average basal values. Animals in groups A and B receiving vincristine and cisplatin scaffold showed no significant change in blood sugar levels, indicating that these drugs are not effective in the body. However, a decrease in blood sugar values is characteristic of granuloma venereum. In this case, hypoglycemia may be due to excessive use of glucose by cells, release of insulin-like growth peptide, or some changes in the normal compensation process against fasting hypoglycemia (**Tella *et al.*2004**). In Group A animals, no significant (P>0.05) changes in blood urea nitrogen concentration were found, but concentrations were within physiological limits. An increase in blood urea nitrogen was observed in group B animals until the fourth week (P<0.05). There was no significant change in blood urea nitrogen of animals in Group A at different times; this shows that the drug has no effect on the kidneys and liver. **Terra *et al*.** (**2004**) **and Sharma *et al*. (2011**) also found no significant change in BUN levels after vincristine stent therapy in dogs with CTVT (P>0.05).

A significant (P>0.05) change in serum urea nitrogen was reported in animals of group B. Serum urea nitrogen is used to evaluate the ability of the kidney to remove the nitrogenous waste from the blood. Increased values of BUN are seen in pre-renal causes (shock, congestive heart failure, and adrenocortical

insufficiency), renal causes (damage to 75% nephrons) and post renal causes (obstruction in the urinary passage) and decrease in hepatic insufficiency dietary protein restriction **(Brar *et al*., 2000).**

In the animals of group A, the fluctuating trend in serum creatinine level was observed, however its level was in the normal physiological limit. In the animals of group B significant ($P<0.05$) increase in serum urea nitrogen was observed up to fourth week.

Non-significant change in creatinine level at various time intervals in animals of group A subjected to administration of vincristine scaffolds indicates the no harmful effect of drugs on renal system. **Sharma *et al.* (2011)** have also observed non-significant ($P>0.05$) change in creatinine level in canine CTVT dog following treatment with vincristine. A significant ($P>0.05$) change in value of creatinine was reported in animals of group B. Creatinine is used to evaluate the healthy status of kidney. Increased values of creatinine are seen in renal damage. The observations in the study revealed that vincristine, cisplatin and their scaffolds do not have any deleterious effects on kidney **(Brar *et al*., 2000)**.

There was non-significant ($P>0.05$) change in the level of alanine amino transferase (ALT) and serum aspartate amino transferase (AST) throughout the period of experiment in animlas of group A and B subjected to the administration of vincristine and cisplatin scaffolds. These values were in the normal physiological limit in all the animals of both the groups at different time intervals throughout the period of this study.

AST is found in high concentrations in cardiac and skeletal muscles as well as liver cells. Animals in group A treated with vincristine sulfate had no significant changes in AST over consecutive weeks of treatment; this is consistent with the analysis of **Mello *et al.* (2013)**; **Dan *et al.* (2018)** reported that vincristine did not harm the liver and muscles. In contrast to the current study, **Sharma *et al.* (2011)** found a significant ($P<0.05$) increase in AST values after vincristine treatment in dogs with CTVT until the second week of treatment. ALT is a liver-specific enzyme that is abundant in the cytoplasm of hepatocytes. The liver is one of the main metabolic centers of the body and its cells contain many important enzymes. When the liver is damaged, cell membranes will become more permeable or cell walls will rupture, allowing enzymes to enter the blood vessels and increasing the level in the bloodstream. Therefore, measuring the activities of these enzymes may reflect the integrity of the liver walls and provide an important method for assessing liver damage. Cytoplasmic enzymes such as alanine aminotransferase and aspartate aminotransferase are affected by cell membrane permeability. During the entire experiment, there were no significant changes in blood gamma glutamyl transpeptidase (IU/L) and blood aspartate levels ($P>0.05$) between the two groups of animals, and the blood results were within normal physical limitations. All animals from different groups at different times throughout the study. Serum GGT is found in many tissues, but the main source is the liver. Microsomal (ribosomal and mitochondrial) enzymes such as gamma glutamate dehydrogenase must be damaged in the liver before they can increase. In this study, high blood GGT levels were observed in animals with liver disease; this confirmed the findings of **Kaneko *et al.*** (**2008**). The decrease in serum GGT after the start of treatment in various groups indicates the positive effect of the treatment.

4. CONCLUSION

Based on the limitations of this study, it was determined that the extent of CTVT cell apoptosis at week one and two in animals treated with vincristine sulfate scaffold compared with large cisplatin scaffold was determined, as demonstrated by physical, clinical, and hematological parameters, biochemical and histopathological (H&E staining) studies. Vincristine scaffold is more effective than cisplatin scaffold because it targets the tumor early. This may be because healthy cells have fewer side effects. Vincristine scaffold can be safely used by field veterinarians to treat TVT in dogs.

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Table 1: Mean±SE of heamtobiochemical parameters after administration of vincristine sulphate in animals of group A and cisplatin in animals of group B at different time intervals

Parameters (Mean±SE)	group	Time intervals				
		0week	1week	2week.	3week	4 week
Haemoglobin(gm/dl)	1	11.00±0.23	10.86±0.47	10.22±0.55	10.20±0.46	10.24±0.45
	2	10.24±0.45	10.45±0.23	10.95±0.32	11.12±0.43	11.18±0.43
PCV (%)	1	43.78±1.58	42.25±2.15	40.60±2.45*	39.85±2.98*	40.85±1.67
	2	41.25±2.56	41.30±2.62	41.50±1.26	42.75±1.58	42.65±1.28
TLC(10^3/µl)	1	8.68±0.49	7.90±0.59	7.85±0.56	7.52±0.54	7.58±0.58
	2	9.20±0.35	9.11±0.33	8.95±0.28*	8.85±0.31**	8.62±0.25
Lymphocyte (%)	1	27.50±2.74	31.75±0.44	35.15±2.73*	37.28±1.28*	37.45±1.55
	2	32.50±1.58	34.25±2.26	36.50±1.70*	38.50±1.39	38.70±1.22*
Neutrophils (%)	1	70.50±3.27	71.76±1.75	68.00±2.32	69.00±2.22	70.00±1.81
	2	69.50±1.79	61.35±4.87*	57.75±2.75**	56.25±1.83*	57.80±2.16
Total Protein(g/dl)	1	5.98±1.51	5.52±1.46	5.48±1.40	5.23±0.28	5.27±0.88
	2	6.85±0.11	6.75±0.34	6.55±1.71	6.51±1.32	6.45±1.22
Albumin (g/dl)	1	3.15±0.40	3.00±0.46	3.20±0.50	3..32±0.61	3.35±0.44
	2	2.54±0.57	2.43±0.62	2.55±0.71	2.35±0.44	2.23±0.76
Glucose(mg/dl)	1	74.40±2.85	69.75±2.462	61.50±3.58	70.65±2.28	75.25±3.18
	2	81.40±6.32	89.50±8.25	85.80±4.89	83.60±6.24	85.60±6.16
Blood urea nitrogen(mg/dl)	1	29.50±2.35	29.75±1.68	30.15±2.56	30.21±1.57	31.01±1.32
	2	30.00±2.83	30.75±2.96	30.45±2.67	31.25±3.15	30.40±2.27
Creatinine(mg/dl)	1	1.16±0.19	1.20±0.44	1.26±0.47	1.25±0.84	1.27±0.32
	2	1.20±0.06	1.35±0.19	1.34±0.24	1.29±0.37	1.26±0.72
AST (IU/L)	1	37.25±1.44	37.65±3.29	38.10±3.05	38.22±1.05	38.25±1.02
	2	40.25±4.82	41.00±4.43	41.90±4.52	41.75±4.56	41.25±4.13
ALT(IU/L)	1	29.50±3.13	28.50 ± 3.03	28.75± 3.46	30.00± 2.45	31.25± 3.12
	2	31.00± 2.45	30.25± 3.44	31.50± 3.76	31.95± 2.55	31.75± 2.45
GGT(IU/L)	1	4.25± 0.54	4.15± 0.75	3.45± 0.60	3.95± 0.50	4.50± 0.80
	2	3.20± 0.69	4.25± 1.47	3.50± 1.47	4.25± 0.88	4.10 ± 0.89

* Significant at $p < 0.05$ difference with 0-week time interval
** Significant at $p < 0.01$difference with 0-week time interval

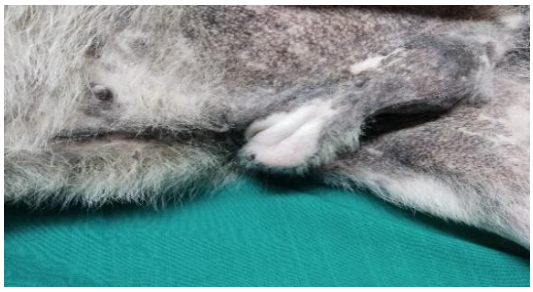

Fig (a)

Fig (b)

Group A: Before and after treatment with vincristine sulphate Scaffolds

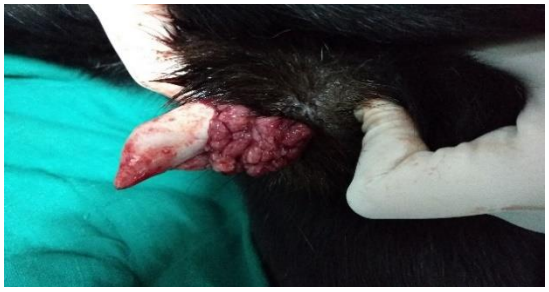

Fig (c)

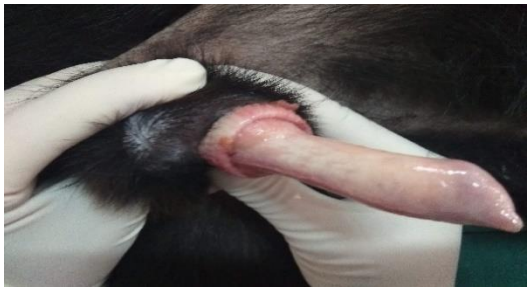

Fig (d)

Group A: Before and after treatment with vincistine scaffolds

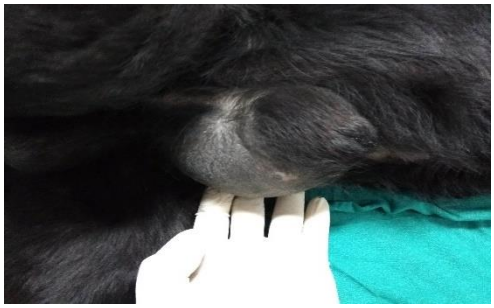

Fig (e)

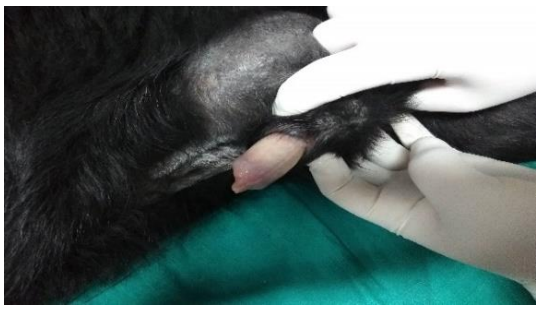

Fig (f)

Group B: Before and after treatment with cisplatin scaffold

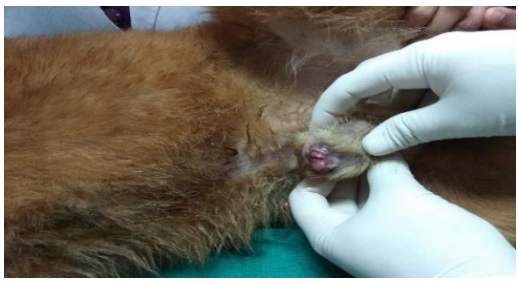

Fig (g)

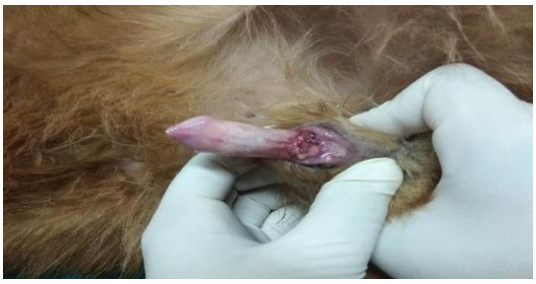

Fig (h)

Group B: Before and after treatment with cisplatin scaffold

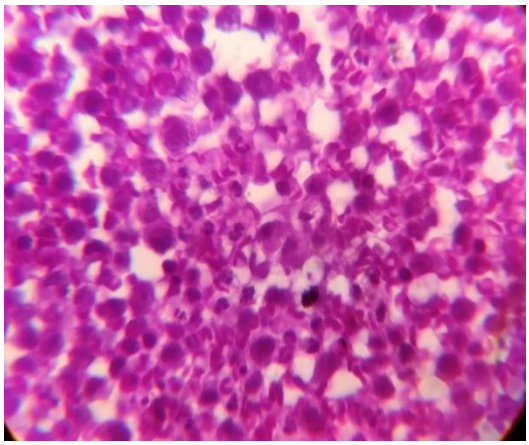

Fig. 1: Group A (0 week)

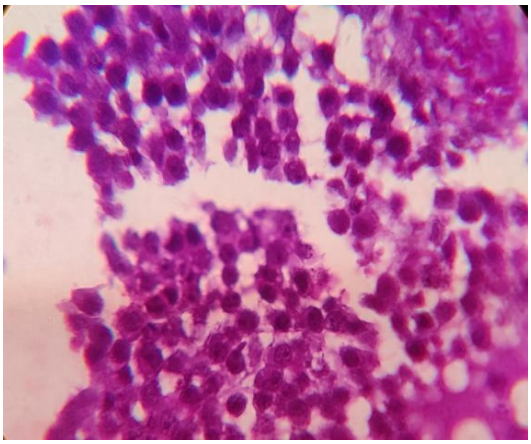

Fig. 2: Group A (3 week)

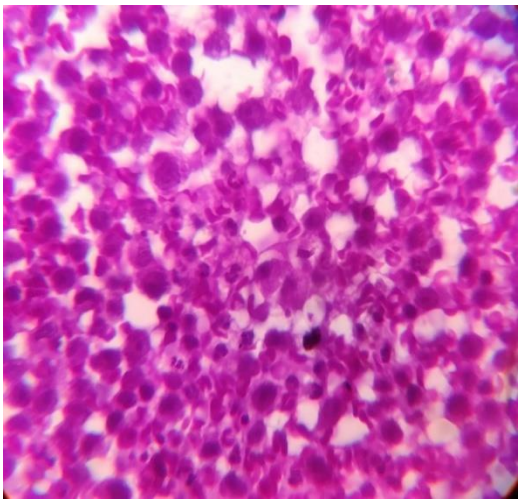

Fig. 3: Group B (0 week)

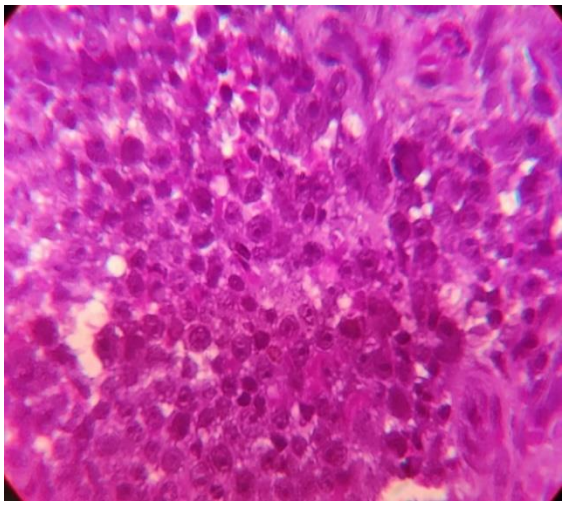

Fig. 4: Group B (3 week)