한국임상수의학회지 15(1) : 214-218 (1998)
Korean J. Vet Clin Med. 15(1) : 214-218 (1998)

# Vincristine Therapy for Canine Transmissible Venereal Tumor in a Jindo Dog

**Chae-Woong Lim[1], Sung-Jin, Cho* and Ju-Young Song****
*Bio-Safety Institute, Chonbuk National University,*
**Family Animal Clinic, **Song's Animal Hospital*

# Vincristine을 이용한 진도견의 전파성 생식기 육종 치료

임채웅[1] · 조성진* · 송주영**
전북대학교 생체안전성 연구소,
*가족동물병원, **송가축병원

**요 약 : 2세의 암컷 진돗개가 3개월간 혈액성 질분비물과와 외음부 종창을 주증으로 내원하였다. 질에 형성된 종괴는 조직병리학적 검사로 개 전파성 생식기 육종으로 진단되어 vincristine sulfate(0.5 mg/M$^2$)을 1주 간격으로 3회 정맥주사를 실시하면서 혈액, 병리조직 검사를 병행하였다. 종괴의 크기는 투여 후 1주부터 급격히 감소되었으며 조직소견상 종양세포는 세포질의 공포변성, 핵농축 및 붕괴, 혹은 apoptosis가 관찰되었다. 4주째 종괴는 완전히 소실되어 치료를 중단하였고 혈액학적 검사 결과 부작용은 없었다. 마지막 투여후 10주째 건강한 새끼 4마리를 자연 분만하여 개 전파성 생식기 육종에서 vincristine 단독 투여로 우수한 치료효과를 얻었다.**

***Key words*** : Jindo dog, transmissible venereal tumor, vincristine chemotherapy

## Introduction

Transmissible veneral tumor (TVT), a naturally occurring contagious neoplasm of dog, affects the external genitalia of both sexes. TVT can be transmitted to dogs, either by coitus or the social licking of external genitalia, or by viral-like particles[4,10]. The venereal tumor in extragenital sites are probably caused by biting and scratching, which predisposes the skin to tumor cell implantation[21]. It was found only in sexually mature dogs and there was no sex predisposition[3]. The tumor, characterized by an undifferentiated, rounded-cell neoplasm, is generally benign and regresses spontaneously. Metastases have been reported in the lymph nodes, liver, skin, eye and brain[1,6,22,24], although metastasis may occur rarely.

There were several approaches to the treatment of TVT, which were surgical removal and radiotherapy. Surgical excision of the tumor proved only partially successful as recurrence of TVT was reported in 27~38 % of cases[7,12]. Radiotherapy was reported to be highly effective but required highly costed-equipment and trained personnel. Although those treatments have been partially or fully successful, chemotherapy is now considered the treatment of choice[3,5,8,11,13].

This study was undertaken to evaluate the efficacy of a antineoplatic drugs, vincristine, for the treatment of TVT in a Jindo dog, with assessment of the sequential clinical and histopathological changes during therapy.

## Case

A 2 year-old female Jindo dog was presented to an Animal hospital, Chonju, because of swelling of external genitalia, vaginal bloody discharge, and dys-

[1]Corresponding author.

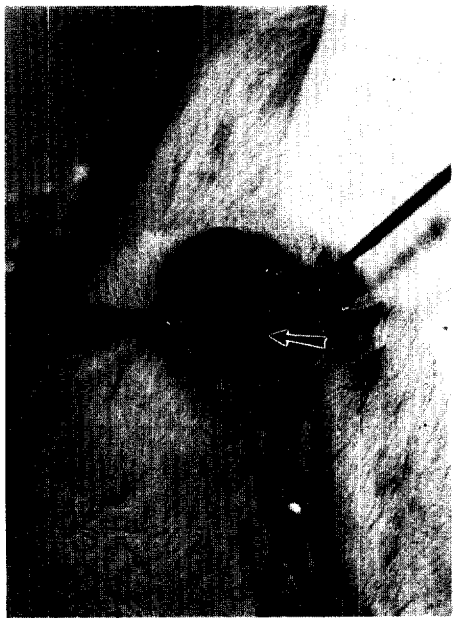

**Fig 1.** Tumor grows exophylic fashion and is located at the ventral wall of vaginal mucosa (arrow).

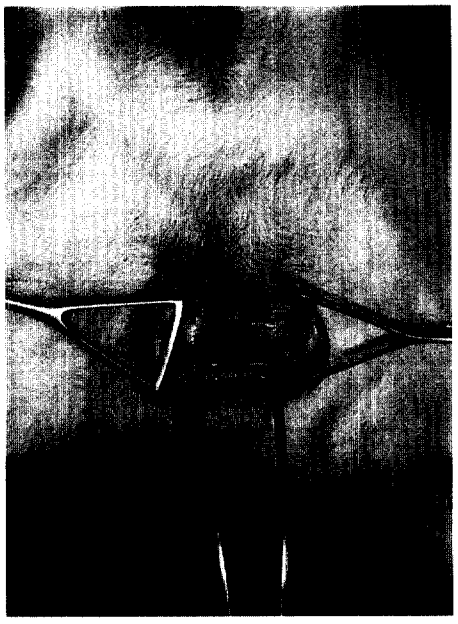

**Fig 2.** Tumor mass are disappeared after chemotherapy.

uria. Three month previously, the dog had been undergone antibiotics several times by other veterinarian without any effects.

On the initial examination, the dog appeared to be thin but the general condition was considered normal. The inflammatory exudates tinged with hemorrhage were discharged from vagina. The masses were firmly palpated within vagina. These were exophylic nodular to multilobulated mass varing size in diameter on the vaginal mucosa and some of superficial part were ulcerated and hemorrhagic (Fig 1).

The dog was underwent hematology, cytology (fine needle aspiration for Diff-Quick stain), and histopathology (tissue biopsy for Hematoxylin and Eosin stain). The patient was initially treated with Trimethoprim-sulfonamide (30 mg/kg, q12h, PO)and Chymotrypsin for 3 days.

Microscopic evaluation of cytological preparations revealed that the nuclei of tumor cells were round to oval shape with eccentrically located 1~2 prominent large nuclei (Fig 3). Histopathologically, the tumor cells formed compact sheets along collagen stroma. The tumor cells were round to oval with a large nucleus contained coarsely scattered chromatin and us-


**Fig 3.** Fine needle aspiration cytology shows the nuclei of tumor cells are round to oval shape. Diff Quick stain, ×200.

ually one eccentrically located prominent nucleolus (Fig 4). Mitotic figures were frequently found. The cytoplasm was faintly granular, light blue and often

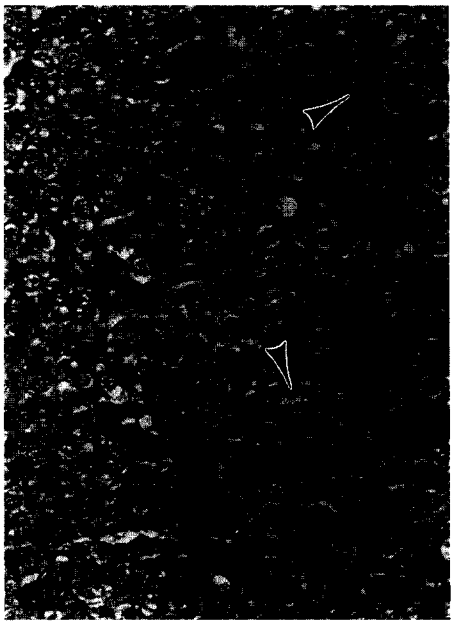

**Fig 4.** Typical transmissible venereal tumor. Tumor cells form compact sheets of lymphoid cells and defined by delicate collagenous stroma. Arrowheads indicate mitotic figures. H&E stain, ×300.

**Fig 5.** The degenerative changes of the tumor cells after chemotherapy. Most nuclei become condensed and cytoplasms are vacuolated. Apoptotic cells are seen (arrowheads). H&E stain, ×300.

contained vacuoles. Hemorrhage and infiltration of the inflammatory cells were additional findings (not shown). Thus, TVT of the final diagnosis was made on the base of the histopathological findings of biopsy.

Thereafter, the dog was given vincristine sulphate, 0.5 mg/M$^2$ intravenously at weekly intervals[10,19,20]. The dose rates were calculated according to body surface area[10]. One week after therapy, tumor reduced in size to half at a rough estimate. Histopathologically, most nuclei became condensed and very irregular in shape and size, ending in karyorrhexis and karyolysis (Fig. 5). The cytoplasm of the degenerating tumor cells was vacuolated. There were the typical apoptotic cells as seen in many regressing tumors. In addition, a few lymphocytes were infiltrated in the tumor. Three weeks after therapy, the tumor had apparently reduced in size and was too small for biopsy.

The hematology performed weekly before treatment to monitor the adverse effects of chemotherapy and no abnomality was noted in the blood count, creatinine values during the therapy (Table 1). The number of WBC was increased before therapy, which was considered to inflammatory reaction on the tumor masses.

**Table 1.** Hematology and creatinine values in the dog treated with vincristine

| | Vincristine Sulfate (0.5 mg/M$^2$ body surface area, IV) | | | |
|---|---|---|---|---|
| | week | | | |
| | 0 | 1 | 2 | 3 |
| HCT (%) | 31.0 | 31.5 | 31.0 | 33.6 |
| HB (g/dl) | 10.7 | 10.1 | 10.3 | 10.9 |
| WBC (×10$^3$/μl) | 22.0 | 18.7 | 16.4 | 6.5 |
| Grans | 17.3 | 16.0 | 14.1 | 4.8 |
| L/M | 4.7 | 2.7 | 2.3 | 1.7 |
| PLT (×10$^3$/μl) | 407 | 289 | 695 | 554 |
| Creatinine (mg/dl) | 0.88 | 0.79 | 1.01 | 0.85 |

Four weeks after treatment, the tumor was regressed completely (Fig. 2). This picture was taken 2 month later after her delivery. The dog did not showed any side effects during therapy. Thereafter, she allowed to run free and was pregnant. She delivered normally 4 healthy puppies by 10 weeks after the therapy was stopped.

## Discussion

TVT occurs in many countries of the world, especially in tropical and subtropical regions and in free roaming dog populations[2,9,15,17,18]. Treatment for this tumor include surgical excision, radiation therapy and chemotherapy. However, there were high recurrence in surgical excision and appropriate facilities in radiation therapy[1,7,12].

Anticancer chemotherapy is a relatively new branch of veterinary medicine until recently. The use of chemotherapy in veterinary practice is expanding as the success of anticancer chemotherapy in companion animals[5,8,10,19,20,23]. In most circumstances the use of a combination of cytotoxic drugs is more effective than a single agent due to tumor cell heterogeneity[14,19,20]. But some tumors are highly sensitive to single agent chemotherapy and examples are followed; adrenocortical adenocarcinoma with mitotane, polycythaemia with hydroxyurea, and chronic granulocytic leukaemia with busulphan[10].

Vincristine is a vinca alkaloid derived from the periwinkle plant, *Vinca rosea Linn.* This alkaloid act by binding specifically to tubulin and inhibiting the formation of the mitotic spindle, thus blocking mitosis and causing a metaphase arrest[10,13]. Vincristine is used for hemopoietic neoplasm and immune-mediated or idiopathic thrombocytopenia.

Doses of cytotoxic drugs in this study was calculated as a function of body surface area rather than body weight because the blood supply to the organs responsible for detoxification and excretion is more closely related to surface area than body weight[10].

Four weeks after vincristine therapy, there was complete tumor regression. Similar results have been reported about regressing time after therapy in previous therapy studies[18,23]. Histopathology is one of the best tools for evaluating of antitumor therapy. Vincristine caused nuclei change, which were pyknosis, karyorrhexis and karyolysis after 7 days of treatment. Most of the cytoplasms were vacuolated. This histopathology is consistent with findings from other studies[21,23]. The additional finding of apoptosis is the effective histological indicator of tumor regression and of the efficacy of chemotherapeutic agents.

In the first case of male Jindo with TVT, which was received combination therapy, vincristine, cyclophosphamide and methotrexate, the tumor mass was nearly regressed at 4 weeks after therapy[18]. In this study, however, single chemotherapy, vincristine, was found to be the highly effective drug to treat the canine TVT.

## Conclusion

A 2-year-old Jindo dog, naturally infected with transmissible venereal tumor, was treated with vincristine sulfate at weekly intervals with 0.5 mg/M$^2$ intravenously. The size of tumor dramatically decreased on day 7. Histopathologically, the regressing tumor cells were degenerated with many cytoplasmic vacuoles, and karyorrhexis, karyolysis and apoptosis. There was complete regression of the tumor on 4 week after therapy and the dog showed no ill effects. The dog delivered normally 4 healthy puppies by 10 weeks after the therapy was stopped. This study showed that vincristine chemotherapy alone was the effective drug for the canine transmissible venereal tumor.

## Acknowledgments

This study was financially supported in part by a Research Grant from Bio-Safety Research Institute, Chonbuk National University in 1998 (CNU-BSRI, NO. 98-05). The authors are grateful to Dr. Kim Yong-Jun for valuable suggestions and to Choi Sun-Ho for her service, Chonbuk national university.

## Reference

1. Amber EI, Adeyanju JB. Oronasal transmissible venereal tumor in a dog. Modern Vet Prac 1986; 67: 154.
2. Amber EI, Henderson RA. Canine transmissible veneral tumor: evaluation of surgical excision of primary and metastatic lesions in Zaria-Nigeria. J Am Animal Hospital Assoc 1982; 18: 350-352.
3. Amber EI, Henderso RA, Adeyanju JB, Gyang EO. Single drug chemotherapy of canine transmissible

veneral tumor with cyclophosphamide, methotrexate or vincristine. J Vet Int Med 1990; 4: 144-147.
4. Amber EI, Isitor GN, Adeyanju JB. Viral-like particles associated with naturally occurring transmissible venereal tumor in two dogs: preliminary report. Am J Vet Res 1985; 46: 2613-1615.
5. Brown NO, Calvert C, MacEwan EG. Chemotherapeutic management of transmissible venereal tumors in 30 dogs. J Am Vet Med Assoc 1980; 176: 983-986.
6. Bright RM, Gorman NT, Probst CW, Goring RL. Transmissible venereal tumor of the soft palate in a dog. J Am Vet Med Assoc 1983; 183: 893-895.
7. Brodey RS, Roszel JF. Neoplasms of the canine uterus, vagina and vulva: A clinicopathological survey of 90 cases J Am Vet Med Assoc 1967; 151: 1294-1307.
8. Calvert CA, Leifer CE, MacEwen EG. Vincristine for treatment of transmissible venereal tumor in the dog. J Am Vet Med Assoc 1982; 181: 163-164.
9. Chang SC, Yang CH. Cytology of transmissible venereal tumors in dogs. Taiwan J Vet Med Animal Husbandry 1996; 66: 307-314.
10. Dobson JM, Gorman NT. Chemotherapeutic agents. In: Cancer Chemotherapy in small animal practice, Blackwell Scientific Public. 1993; 52-54.
11. Das AK, Das U, Das D. Clinical report of efficiency of vincristine on canine transmissible veneral sarcoma. Indian Vet J 1991; 68: 575-576.
12. Das LL, Sahay PN. Surgical treatment of canine transmissible venereal tumor-a retrospective study. Indian Vet J 1989; 66: 255-258.
13. Golden DL, Longston VC. Uses of vincristine and vinblastine in dogs and cats. J Am Vet Med Assoc 1988; 193: 1114-1117.
14. Hoque M, Pawde AM, Singh GR. Combination chemotherapy in canine transmissible veneral tumor. Indian Vet J 1995; 72: 973-975.
15. Ivoghli B. Canine transmissible venereal tumor in Iran. Vet Path 1977; 14: 289-290.
16. Jubb KVF, Kennedy PC, Palmer N. The female genital system. In: Pathology of Domestic Animals, 4th ed. Academic Press 1993: 451-453.
17. Kimeto B, Mugera GM. Transmissible venereal tumor of dog in Kenya. Bull Animal Health Prod 1974; 22: 327-329.
18. Kim JM, Yang HK, Shin TY, Kweon OK, Nam TC. A case of chemotherapy for transmissible venereal tumor in a dog. Korean J Vet Clin Med 1996; 12: 212-215.
19. MacEwen EG. Anticancer drugs: dose schedule and guideline. In: Current veterinary therapy XI W. B. Saunders 1992: 402-405.
20. MacEwen EG. Chemotherapy: Pharmacologic and toxicologic considerations. In: Current veterinary therapy XII W.B. Saunders 1995: 478-482.
21. Otomo K, Koike T, Kudo T, Sakai T. Histological and ultrastructural findings of regressing canine transmissible venereal tumor after repeated transplantation. Japan J Vet Sci 1981; 43: 823-832.
22. Parent R. Teuscher E, Morin M, Buyschaert A. Presence of the canine transmissible venereal tumor in the nasal cavity of dogs in the area of Dakar. Can Vet J 1983; 24: 287-288.
23. Singh J, Rana JS, Sood N, Pangawkar GR, Gupta PP. Clinco-pathological studies on the effect of different anti-neoplastic chemotherapy regimens on transmissible venereal tumors in dogs. Vet Res Comm 1996; 20: 71-81.
24. Yang TJ. Metastatic Transmissible venereal sarcoma in a dog. J Am Vet Med Assoc 1987; 190: 555.