

EXTRAGENITAL CANINE TRANSMISSIBLE VENEREAL TUMOURS: A CASE SERIES

**B. M. L.N. Bandaranayaka*, S. Kabilan, K. A. R. K. Perera, C. Abeykoon,
K. A. N. Wijewardena, H. M. S. Ariyaratna**

*Department of Veterinary Clinical Sciences, Faculty of Veterinary Medicine and Animal
Science, University of Peradeniya*

SUMMARY: Transmissible venereal tumour is a contagious tumour frequently found in dogs in Sri Lanka. Generally, canine TVT (cTVT) is transmitted via sexual intercourse and therefore the lesions are typically found in the external genitals of dogs. Due to the characteristic cauliflower-like appearance of gross lesions of cTVT, diagnosis of genital cTVT is mostly easy and straightforward when confirmed by cytology. However, cTVT cells may transplant on mucous membranes other than external genitals due to the social behaviour of dogs and produce atypical lesions at extragenital sites. Extragenital cTVT is difficult to diagnose, especially when the affected dogs lack concurrent genital lesions. Only a limited number of extragenital cTVT case reports are published in Sri Lanka. This report provides a comprehensive description of extragenital cTVT in nine dogs presented with a variety of lesions, diagnosis and response to treatment with vincristine sulphate.

Keywords: Canine TVT, extragenital, vincristine

INTRODUCTION

Transmissible venereal tumour (TVT) is a round cell neoplasm common among dogs in tropical and subtropical regions of the world. The main mode of transmission of canine TVT (cTVT) among dogs is sexual intercourse and as a result, these tumours are frequently present on external genitals (Papazoglou *et al.*, 2001). Genital cTVT has a characteristic cauliflower-like appearance and therefore diagnosis is often simple and straightforward when supported by cytology (Flores *et al.*, 2012). Cytologic preparations of cTVTs include discrete round cells with eccentric nucleus, single prominent nucleolus, and characteristic marginated, clear, punctate cytoplasmic vacuoles (Raghunath *et al.*, 2015). Unlike genital cTVT, extragenital form is mostly resulting from social interactions between dogs such as sniffing, licking, biting, and scratching that facilitates live tumour cell implantation on various non-genital mucous membranes or damaged skin (Cohen, 1985; Das and Das, 2000). Interestingly, as these social behaviours are not restricted to sexually intact dogs, even desexed dogs may contract cTVT. Occasionally extragenital cTVT is produced by metastases of genital cTVT to lymph nodes or other distant organs (Ferreira *et al.*, 2000). Extragenital cTVT lesions are diagnostically challenging, especially when concurrent genital lesions are absent. Similar to genital cTVT, the treatment of choice for extragenital cTVT is also vincristine sulfate. Vincristine blocks mitosis by interfering

with micro tubule polymerization and thereby inhibition of cell proliferation causing cell death (Das and Das, 2000). This report describes a series of extragenital cTVT cases presented to Veterinary Teaching Hospital, University of Peradeniya, Sri Lanka, from January 2021 to January 2022. This series includes six dogs with extragenital cTVT lesions without primary genital lesions, two dogs with extragenital cTVT with primary genital TVT, and one dog with genital cTVT with concurrent regional lymph node metastasis.

Case descriptions

1. Dogs with extragenital cTVT lesions without primary genital lesions

Case 1: A 1 ½ -year old, intact-male, Golden retriever was presented with soft, non-pruritic, ulcerated, approximately 2mm-6mm diameter, cutaneous papules, developed over one month, and intermittent nasal bleeding (Figure 1A). Previously, the dog had been treated by a regional veterinarian for pyoderma with antibiotics for one week without any success. In addition to the skin, papules and nodules were identified on gums, both conjunctivae and upper eyelids, nasal planum, upper palate, ventral abdomen, and medial thighs. No lesions were found on the external genitals. Epistaxis was absent at the time of presentation and except for the mass lesions, general clinical examination (GCE) and complete blood counts (CBC) were unremarkable. The other differentials were

cutaneous histiocytoma, reactive histiocytosis, pyoderma and diverticulitis. Superficial skin scrapings obtained from the cutaneous lesions were unremarkable.

The impression smears prepared from the cutaneous lesions and the smears prepared from the nasal swabs revealed populations of round cells with cytological features consistent with cTVT including an eccentric nucleus, single prominent nucleoli, and margined punctate cytoplasmic vacuoles (Figure 1.A1). After treatment with three doses of vincristine sulfate (0.5 mg/m², q 2 week) skin lesions and nasal discharges got completely resolved.

Case 2: An 8-year-old, intact male, crossbred dog was presented with progressive unilateral, facial swelling for one month. The facial swelling had a soft to firm consistency and contained a single draining tract from which reddish-brown purulent discharge was observed at the time of presentation (Figure 1B). According to the owner, the draining tract on the face was observed after a dog fight. General clinical examination identified a prominent respiratory stertor, moderately pale mucous membranes, hyperthermia, bounding pulse, and moderate generalized lymphadenomegaly. The possible differential diagnoses included nasal adenocarcinoma, lymphoma and severe bacterial/fungal rhinitis. A round cell population with cytological features consistent with cTVT was observed in the fine needle aspiration (FNA) obtained from the facial swelling (Figure 1. B1). The lymph node aspirates obtained from prescapular, and popliteal lymph nodes revealed evidence of reactive lymph nodes. The CBC revealed anemia (Hct=22%, RBC=6.5 x 10⁶/μL, Hb=3.6 g/L), and the blood smear contained *Babesia gibsoni* organisms (average 3-4 per oil immersion field). The dog was initially treated for babesiosis with imidocarb dipropionate (6.6mg/kg) and neutrophilic inflammation with cephalexin (20 mg/kg, bid). Later, cTVT was treated with vincristine sulfate (0.5 mg/m², q 2 week) and antibiotics (cephalexin 20 mg/kg, bid). The facial swelling became approximately half of its original size after two doses of vincristine. In addition, the severity of the stertor and purulent discharges from the swelling were also reduced. However, after the second dose of vincristine the dog was lost to follow-up.

Case 3: An 8-year-old, intact male, crossbred dog was presented with a progressive bilateral, nasal swelling for one month (Figure 1.C). The muzzle area of the dog was severely and diffusely

oedematous, multifocally ulcerated with crust formation. On the surface of the lesion, multiple draining tracts filled with yellow-brown, purulent material were also observed. General clinical examination revealed a prominent respiratory stertor. In addition, both mandibular lymph nodes were moderately enlarged. No other lesions were found elsewhere in the body. The differentials included nasal adenocarcinoma, malignant melanoma, lymphoma, cTVT, and severe bacterial/fungal rhinitis. A round cell population with cytological features consistent with cTVT was observed in the FNAB obtained from the nasal swelling (Figure 1.C1). After two doses of vincristine sulfate (0.5 mg/m², q 2 week) and antibiotics (cephalexin 20 mg/kg, bid), the nasal swelling became approximately one third of its original size and the intensity of the stertor was also reduced. However, after the third dose of vincristine the dog was lost to follow-up.

Case 4: A 3-year-old, crossbred, neutered female dog was presented for dome shape, approximately 2.5 cm diameter, cutaneous mass with surface ulcerations on the dorsal paw area of the right foreleg (Figure 1. D). Except for the moderate lymphadenomegaly in the ipsilateral prescapular lymph node, the GCE was unremarkable. The differentials included histiocytoma, mast cell tumour and lick granuloma. Impression smears prepared from the surface of the lesion revealed many degenerating neutrophils admixed with cellular debris. The FNAB collected from the lesion showed a population of round cells of which the cytological features were consistent with cTVT (Figure 1. D1). Tumour cells were not observed in the FNABs obtained from the enlarged prescapular lymph nodes. After the treatments with two doses of vincristine sulfate (0.5 mg/m², q 2 week) the cutaneous mass disappeared completely leaving only a scar.

Case 5: A 2-year-old, crossbred, neutered female dog was presented for a non-ulcerated, approximately 2 cm in diameter, cutaneous nodule in the caudoventral abdomen for three weeks (Figure 1.E). Except for the nodule, the general clinical examination was unremarkable. The differentials considered were histiocytoma, cTVT, and foreign body granuloma. The FNAB obtained from the nodule revealed a population of round cells with morphological features that were consistent with cTVT cells (Figure 1. E1). After treatments with two doses of vincristine sulfate (0.5 mg/m², q 2 week), the mass disappeared completely.

Case 6: A 6-year-old, intact male, crossbred dog was presented with a progressive, facial swelling for 1 ½ months. The facial swelling was regionally extensive on the left side of the face, compressing the left eye and spanning to the forehead area (Figure 1.F). The swelling had a soft to firm consistency and the skin over it was intact. Although compressed by the swelling, the vision of the left eye was unremarkable. On general clinical examination, a prominent respiratory stertor, and moderately enlarged bilateral, mandibular lymphadenomegaly were detected. The possible differential diagnoses were nasal adenocarcinoma, lymphoma, malignant melanoma, cTVT and severe bacterial/fungal rhinitis. A round cell population with cytological features consistent with cTVT was observed in the FNAB obtained from the facial swelling (Figure 1. F1). After treating with vincristine sulfate (0.5 mg/m², q 2 week) and antibiotics, facial swelling became approximately half of its original size. After the third dose of vincristine sulfate, the swelling became one-fifth of its original size and the respiratory stertor disappeared. The dog was lost to follow-up after the third dose of vincristine sulfate.

2. Cases with extragenital cTVT lesions with primary genital TVT

Case 1: A 14-year-old, crossbred, intact male dog was presented with a perineal swelling developed over 6 months (Figure 2. G). As revealed by per rectal examination, the anal opening of the dog has deviated to the left side due to a pelvic mass. The perineal swelling was suspected to be an extension of the caudal intra-abdominal mass. Attempts to urinary catheterisation revealed that the urethra was not patent. Additionally, multiple, firm, variably sized, cutaneous nodules were detected on the prepuce. A mass with soft tissue opacity occupying the entire caudal abdomen and the perineum was identified in lateral abdominal radiographs. An ultrasound-guided FNAB from the intra-abdominal mass showed a population of round cells with cytological features consistent with cTVT (Figure 1. G1). Complete blood count revealed moderate leukocytosis (WBC = 33.8 x 10³/μL), and erythrocyte and platelet counts were within the normal limits. The impression smears prepared from

the penile nodules also showed a similar population of round cells identified in the FNAB. The dog was treated with intravenous vincristine sulfate (0.5 mg/m²) and supportive therapy. After the initiation of chemotherapy, the dog was lost for follow-up and later it was reported that the dog died two weeks after the commencement of chemotherapy.

Case 2: A 2-year-old, female, cocker spaniel was presented for pregnancy diagnosis. Abdominal ultrasound examination revealed two dead and one live immature fetuses. General clinical examination revealed multiple, variably sized, fragile, pink-grey masses located around the anal opening and vagina (Figure 2. H). The impression smears prepared from the peri-anal and vaginal lesions were similar and revealed a population of round cells with cytological features consistent with cTVT (Figure 2. H1). A cesarian section was performed to remove the fetuses. Two weeks after the surgery chemotherapy with vincristine sulfate (0.5 mg/m², q 2 weeks) was initiated, and after two doses of vincristine, all perianal and vaginal lesions completely disappeared.

3. Cases with metastatic cTVT

Case 1: A 3 ½-year-old, crossbred, intact female dog was presented for bloody vaginal discharges observed for two days. General clinical examination revealed a cauliflower-like vaginal growth. In addition, two firm, non-ulcerated, inguinal masses (0.5 cm and 0.7 cm diameter) suspected to be enlarged inguinal lymph nodes (Figure 2. I) were also detected. Except for the abnormal vaginal growth and the inguinal masses, the GCE was unremarkable and in the CBC all parameters were within the normal limits. Impression smears prepared from the vulval lesions revealed a population of round cells with cytological features consistent with cTVT. The FNABs obtained from the inguinal lesions revealed many round cells with consistent cytological features of cTVT admixed with small and medium-size lymphoid cells and macrophages (Figure 2. I2). The dog was treated with vincristine sulfate (0.5 mg/m², q 2 weeks) and all lesions disappeared after two doses.

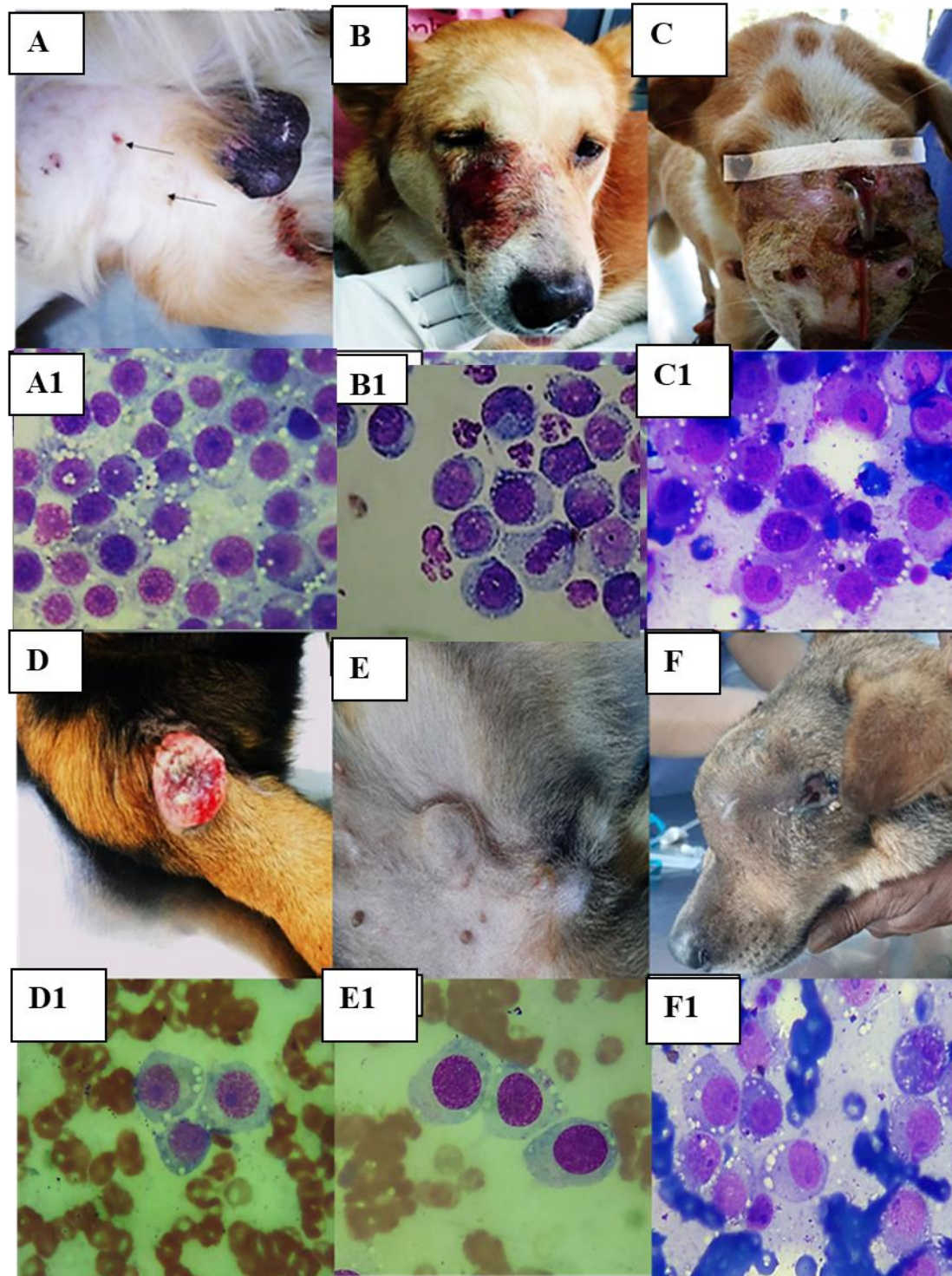


Figure 1: Gross pathology of extragenital cTVT lesions. A: Cutaneous papules in the ventral abdomen. B: Unilateral facial swelling with a draining tract. C: Multiple draining tracts around the nasal planum. D: Ulcerative and dome shape cutaneous lesion. E: Cutaneous nodule on the caudo-ventral abdomen. F: Facial swelling almost completely obliterating the left eye. Cytology A1, B1, D1, E1, Leishman stain is used to stain all cytology smears except C1 and F1 (Dif-Quik). All images are taken using oil immersion x100.

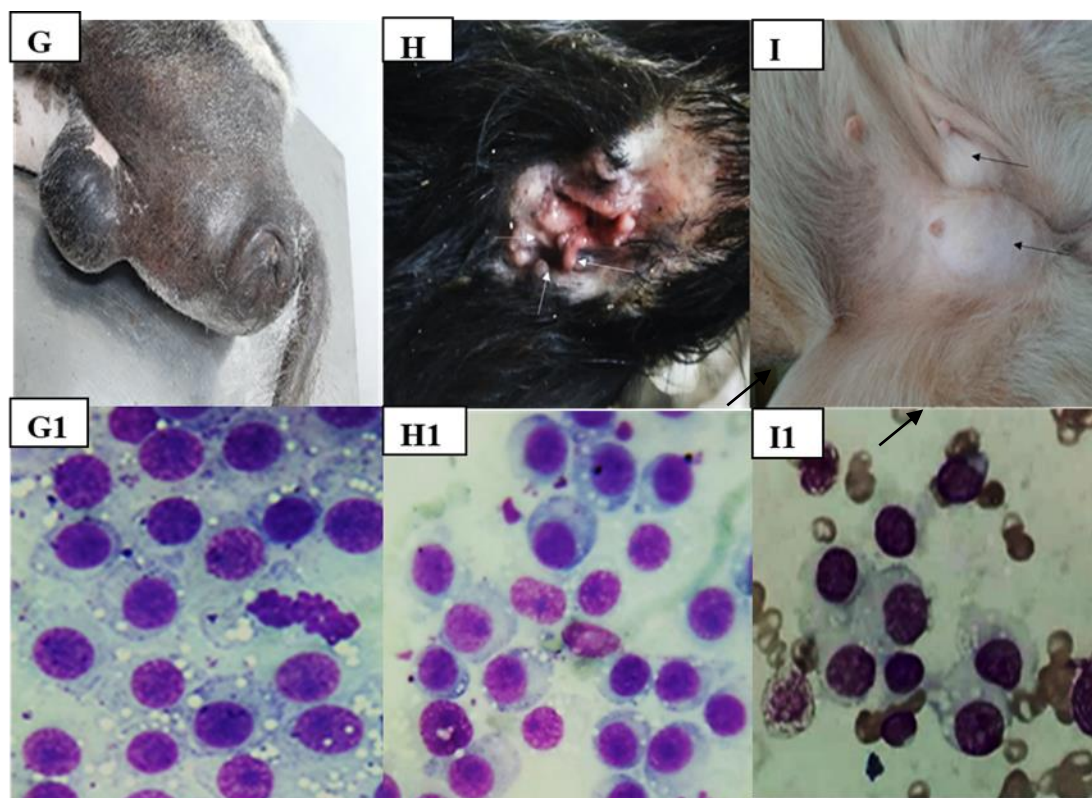


Figure 2: G: Enlarged perineal region. H: Nodular lesions around the anal opening (white arrows). I: Enlarged inguinal lymph nodes due to cTVT metastasis (black arrows). Cytology: Leishman stain is used to stain all cytology smears and all images (G1, H1 & I1) are taken using oil immersion x100.

DISCUSSION

Extragenital cTVT is uncommon and there are only a limited number of published case reports available in literature. Further, case series of extragenital cTVT are less frequent than single case reports. To the authors' knowledge, there are only a few published case reports of extragenital cTVT in Sri Lanka (Perera *et al.*, 2021). This report provides a comprehensive description on a series of extragenital cTVT cases with variable presentations. According to the previous literature, the most common extragenital locations of cTVT are nasal cavity, eye, and skin or subcutaneous tissues. Sub mandibular, cervical and inguinal lymph nodes were shown to contain TVT metastases frequently (Chikweto *et al.*, 2013). In addition to the common sites of extragenital cTVT described previously, the present report includes some uncommon sites of extragenital cTVT including, gums, nasal planum, upper palate and anus.

The typical cauliflower appearance was lacking in almost all the extragenital cTVT lesions described in this report. Further, the vast morphological variability of the extragenital cTVT lesions of the

dogs included in this report suggest the difficulty of initial identification of such lesions as cTVT or possible misdiagnosis of cTVT by the veterinarians in TVT endemic countries such as Sri Lanka. The authors suggest that the awareness regarding the diverse nature of the extragenital cTVT lesions and the use of in-house cytology would be useful to avoid misdiagnosis of extragenital cTVT and thereby prevent or minimize treatment failures.

The response to vincristine sulphate was good in a majority of the extragenital cTVT cases described in this report. Only a single case did not respond to vincristine therapy. This case was presented late and probably had disseminated TVT at the time of presentation which could have contributed to the lack of response to treatment with vincristine sulphate. Vincristine sulfate is the drug of choice for cTVT and only rarely reported to be non-responsive (Hantrakul., 2014). Other round cell tumours except lymphoma are not shown to be sufficiently responsive to vincristine sulphate used as the sole treatment (McCaw *et al.*, 2008; Rusbridge *et al.*, 1999). For canine lymphomas too, use of vincristine

alone is rarely practiced as it is less effective (Wang *et al.*, 2016).

The cytomorphology of the cases included in this report were characteristic of cTVT cells. However, no immunocytochemistry or immunohistochemistry was performed to completely rule out the possibility of other round cell tumours due to financial constraints which is a limitation of the current report. In summary, this report describes some uncommon presentations of extragenital cTVT that would be helpful for the veterinarians in endemic countries to include cTVT as a differential diagnosis for similar lesions in dogs presented to them.

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