Canine Transmissible Venereal Tumour (TVT)

SUMMARY

Canine Transmissible Venereal Tumour (TVT) is reviewed, **based on** clinical data of more than **500 cases recorded** in our Clinic during the last **25 years**, with special reference to its treatment with **vincristine.**

INTRODUCTION

Canine transmissible venereal tumour (TVT) or Sticker's sarcoma was first described by Hujard in 1820 in Europe and its name has been associated with Sticker who systematically studied it in the beginning of the 20th century. It is a neoplasm with unusual properties and unconventional clinical development, naturally occurring exclusively in dogs contaminated primarily by sexual contact and possibly by direct contact related with social behaviour (e.g., sniffing, licking of the genitalia, bite wounds during fights). It is almost always located at the genitalia of both sexes and is rarely found elsewhere in the body, while it metastasises in only a very few cases. Transmission occurs by inoculation of intact neoplastic cells in the damaged mucosa or skin.

For more than a century, TVT has attracted the attention of many authors, stimulated by a) the high frequency of its occurrence and the necessity of finding effective treatments, b) the peculiar features of the disease, c) the continuously increasing interest of human and veterinary medicine in oncology and d) the possibility of using dogs for experimental manipulations, hardly feasible in human beings.

GEOGRAPHICAL DISTRIBUTION

TVT has been recorded in all continents during the 20th century; Asia (Wong & K'Ang 1932), America (Bloom et al 1951), Africa (Bwangamoi 1967) and Australia (Locke et al 1975); yet this does not mean that it was previously absent from those regions.

TVT is seldom or no more detected in North and Central Europe and in North America, mainly due to the population control of stray animals, the preventive pre-breeding examination and the effective treatment of clinical cases. With a few exceptions, TVT remains endemic in the rest of the world, obviously because of the uncontrolled population of stray dogs and the inadequacies of exerting effective treatments.

AETIOLOGY AND TRANSMISSION

The transmission of TVT by means of intact neoplasm cells was assumed already from the beginning of the 20th century (Sticker 1905). Later, it was proven that the dog is the only host of TVT (Bloom 1954). Then it was confirmed that the mutated neoplasm cell itself was the causal agent of TVT and that it induces an immune response in the host (Cohen 1972, 1978).

Significant morphological differences have been repeatedly demonstrated to exist between normal dog cells and cells of the tumour. These include constantly some highly specific chromosome aberrations, which, when associated with other factors, lead to the conclusion that TVT derives from cells that have undergone a mutation caused by a still unknown factor. Tumour cells are exfoliated and transplanted during coitus from animal to animal and perpetuate themselves like any other heterologous, mono-cellular organism. The mechanism allowing the neoplastic cells to override nature's histocompatibility barrier is unknown, while the presence of active immunity has been demonstrated.

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CLINICAL OBSERVATIONS

The clinical appearance of TVT has been repeatedly described and is well known. Findings from the majority of cases, recorded in our clinic are summarised below:

Gender and age of infected dogs: Females were infected more often than males (64.5% and 35.5%, respectively). The disease usually (80%) occurred in animals of reproductive age (2 to 8 years old) and less often at older ones.

Main duty--use and social habits of dogs: The main depots of TVT are considered to be populations of unsupervised stray and semi-stray dogs and owned dogs with vague symptoms. Any close contact with those dogs increases the risk of infection. High-risk groups included especially the habitually yard-escaping dogs (75.5%), usually guard dogs (41.3%) and hunting dogs (41.5%), which often came in proximity at the hunters meeting points. TVT was rare in "strictly" supervised home-kept companion animals (4%), occurring only after escape to experience an uncontrolled-unwanted copulation.

Tumour location: In female dogs the neoplastic lesions were usually located at vestibule (95,6%) and less often at the vagina (44.5) or invading the vulvar lips (18.6%). Main lesions were almost always present at the junction of the vestibule and vagina, perhaps due to the high pressure exerted on this area during mating.

In male dogs neoplastic lesions were usually located on the more caudal part (bulbus glandis, 81.5%) and less often on the shaft (pars longa glandis, 25.9%) or the tip (9.9%) of the glans penis. Neoplastic lesions, when detected on the preputial mucosa (internal lamina, 19.8%) were always concurrent with those of the glans penis, in contrast to others reports.

Common symptoms: The commonest clinical signs observed included a serosanguineous or pure hemorrhagic vaginal or preputial discharge (94.6%), protrusion of the neoplastic lesions (31.3%) and deformation of the external genitalia (30.4%). The peculiar odour of the neoplastic lesions discharge (27.2%), which after secondary bacterial infection became particularly unpleasant, and the excessive licking (5.8%) of the genitalia were also signs often reported by keen owners. Other less common symptoms were dysuria (5.4%), weakness (4.6%), ulcers in the perineum area (2.1%), anorexia (1.7%), constipation (0.8%), paraphimosis (0.8%), mating refusal (0.4%) and weight loss (0.4%). It is clear that clinical findings were less striking in male dogs and the disease was consequently less easily perceptible than in females. Furthermore, in male dogs, there are cases where TVT was accidentally found during other clinical examinations. Clinical findings as well as haematological and biochemical evaluations strongly suggest that the general health of affected animals was not impaired unless the tumour became necrotic and infected or occluded the urethral orifice, or metastasised.

Hematocrit values were slightly lower than normal in less than 10% of the affected dogs, but no severe anaemia was found, as also reported by other authors. The white cell count was higher than normal in about 30% of the cases; most dogs showed a mild to moderate leukocytosis, probably caused by the inflammation of the tumour surface.

Tumour growth and spread: The time from infection to admission of the dog seems to influence the size of the tumour. During the first six months after infection, the local genital expansion of the neoplasm differed among animals. Thus, there were cases in which the neoplasm was barely perceptible and others in which it expanded and severely corrupted the external genitalia. However, from the study of long-existing untreated cases (presenting only mild symptoms) it was found that the extent of neoplastic lesions on the genitalia was closely related to the time elapsed from the onset of the disease (i.e., the neoplasm continued to grow). More specifically, TVT appears to progressively expand until covering most of the external genitalia. Then, it develops more slowly or it may show alternate periods of progressive growth and partial regression. According

to our observations on naturally occurring TVTs, none of them had shown spontaneously a complete regression but they persisted at least for a period of 3-4 years without severe consequences to the animal's health. The diversity in the local distribution or extension of the neoplastic lesions on the genitalia was not found related to factors like animal's breed, age, gender, usage, or general health condition.

On the contrary, the frequency of occurrence of metastases seems to be affected by the gender. Indeed, metastases were more frequent in male (15.6%) than in female dogs (1.8 %). In the majority of the cases, regional lymph nodes were affected, while only a few cases developed metastases in the parenchymal organs or at the skin. Metastases occurred irrespective of the age of the affected animal and, in contrast to most neoplasms, they usually appeared at the first stages of TVT development. Interestingly, animals with metastases when compared to those without metastases showed larger sizes of genital lesions, though the same time had elapsed from the disease onset in each case.

Sometimes the course of the disease was rapid, dramatic or even fatal in metastatic TVT cases. Such severe incidences appeared more frequently in stray, distressed or unhealthy animals, possibly because of a reduced immune response. Common examples refer to animals, which were simultaneously suffering from immunosuppressive diseases (e.g., ehrlichiosis) and/or were subjected to immunosuppressive doses of corticosteroids.

According to our experience neoplastic focuses on genitalia could always be detected in cases where any extragenital TVT lesion was present. Therefore, such cases should be considered as metastases from the primary genital focus. However, other authors have reported that the buccal and nasal mucosa, as well as the skin could be also primary focuses, as a result of the dogs' social behaviour.

Some dogs that had been definitely cured from TVT by radiotherapy and/or chemotherapy became re-infected two or more years later. This fact leads to the conclusion that precedent TVT infection does not provide long-term immunity.

TREATMENT

At present, surgical treatment, chemotherapy and radiotherapy are used to treat TVT, while immunotherapy has not been proven effective.

Surgical treatment has been applied since the last century (Wong & K'Ang 1932) with a low rate of efficacy (30-35% relapses due to tumour cell transplantation into the surgical wound during operation). The use of electrocautery makes the operation easier and seems to be a little more effective; however it is still far from being suggested as the first choice. Therefore, surgical treatment might be applied to those dogs that present solitary, small, easily accessible and noninvasive tumour nodules.

TVT has been proven to be highly sensitive to irradiation, already from the last century, (Wong & K'Ang 1932). Solacroup proposed radiation therapy for TVT in Europe in 1950, which has been employed since, mainly in France resulting in a sufficient up to date incidence reduction of TVT cases. Dosage recommendations range from 1500 to 2500 rads (depending on the chronicity and the extension of neoplastic lesions), divided in sessions of 400-500 rads over a period of 1-2 weeks, or a single dose of 1000 rads which, if not curative, can safely be repeated 1-4 times. However, radiotherapy lacks practicality due to requirements like trained personnel, specialised equipment and expenses. Therefore its use is recommended in cases where other treatments fail.

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Sticker was the first who attempted TVT chemotherapy (arsenicals) at the beginning of the 20th century. The trials with new generation--antineoplastic drugs started during the 6th decade (Deschanel 1962) and vincristine, which was destined to become the drug of choice for TVT therapy, was included in treatment protocols since the 8th decade (Broadhurst 1974).

Currently, the intravenous administration of vincristine at the dose of 0.6 mg/m2 of body surface, once a week, for 2-6 weeks, is the treatment of choice, irrespective of a) the neoplasm size--extent; b) the presence of metastases; and c) the duration of the disease. The time needed to complete treatment and the expenses involved are within reasonable limits. The animals fully recover, with no impact on behaviour and reproductive ability.

Based on our experience, we can raise the following interesting points:

Dogs being infected for less than 1 year, i.e., TVT at initial stages of progression are easily treated. The presence of metastasis, the gender or the age of the animals treated do not influence the duration of chemotherapy. Metastasis subsidence concurs impressively.

Chronic cases infected for more than 1 year may resist to treatment, thus demanding therapy of longer duration without ensuring successful results. In case of failure, radiotherapy gives excellent results; alternatively doxorubicin chemotherapy may be applied.

The potential for a successful vincristine treatment becomes markedly limited when treatment course is interrupted for 2 weeks or more.

The presence of small size tissue remnants (of less than 0.5 cm), which do not bleed after being rubbed, must not be a reason to continue treatment.

Temporary side effects (partial anorexia, mild depression) may be reported in less then 20% of the treated dogs, usually 1-2 days after vincristine administration. Chemotherapy **may cause a decrease of** the white blood cell count (transient leukopenia), but only a few cases (less than 2%) present such a leukopenia that might deserve an adjunctive antibiotic treatment or impose suspension (discontinuation) of one or more chemotherapeutic administrations.

Before initiating vincristine chemotherapy, it is important to assess the general health condition of the animal while during therapy it is necessary to follow up the total number of leukocytes, at least at weekly intervals.