TRANSMISSIBLE VENEREAL TUMOUR IN DOGS

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Transmissible venereal tumour (TVT) in dogs is a naturally occurring tumour transmitted from animal to animal during copulation by viable tumour cells that mainly affects the external genitalia and occasionally the internal genitalia.

TVT has been recorded all over the world and in India incidence of TVT in dogs is reported to range from 23-43 %. A large stray dog population and uncontrolled sexual behavior appear to be one reason for high incidence of TVT. The tumour is seen most commonly in sexually active male and female dogs (2-8 years of age) allowed to roam freely. Females are infected more often than males.

Etiopathology

Although a viral cause has been postulated but not verified, recent research confirms that the tumour is clonal in origin, and the development of this tumour requires transmitting the neoplastic cells from one dog to another.

The exfoliation and transplantation of neoplastic cells during coitus or physical contact provide the main mode of transmission onto genital mucosa, and also onto nasal or oral mucosa, during mating or licking of affected genitalia, respectively. The implantation of the tumour is facilitated by the presence of any mucosal lesion or by the loss of mucosal integrity.

The tumour growth appears 15 to 60 days after implantation. TVTs are immunogenic tumours, and the immune system of the host has a main role in inhibiting tumour growth and metastasis. Metastases have been reported in less than 5–17% of cases and described in subcutaneous tissue, skin, lymph nodes, eyes, tonsils, liver, spleen, oral mucosa, hypophysis, peritoneum, brain, and bone marrow. Extragenital lesions occur both in isolation and in association with the genital lesions. Although, spontaneous remission has been described in experimental transplantation it has not been confirmed in natural cases.

Clinical Signs/Symptoms

The commonest clinical signs observed include a serosanguineous or pure hemorrhagic vaginal or preputial discharge, protrusion of the neoplastic lesions and deformation of the external genitalia.

TVTs are single to multiple, pink-red, nodular, papillary multilobulated, cauliflower-shaped or pedunculated lesions that vary greatly in size and can exceed up to 15 cm diameter when progress deeper into the mucosa. Neoplasms are relatively firm but fragile; the superficial part is commonly ulcerated and inflamed and bleeds.

In female dogs the neoplastic lesions are usually located at vestibule, often at the junction of the vestibule and the vagina perhaps due to the high pressure exerted on this area during mating. It sometimes surrounds the urethral orifice and, if it is just within the vagina, it may protrude from the vulva.

In male dogs the tumour is usually located on the caudal part (bulbus glandis) and less often on the shaft (pars longa glandis) or the tip of the glans penis and occasionally on the prepuce. Neoplastic lesions, when detected on the preputial mucosa are concurrent with those of the glans penis.

The serosanguinous or haemorrhagic discharge may be confused with estrus, urethritis or cystitis and, in the male with prostatitis. In older dogs, the differential diagnosis must also include urinary bladder and urethral neoplasms. The tumour can cause mechanical obstruction to the flow of urine, dystocia in whelping females and phimosis or paraphimosis in the male.

The general health of affected dogs is not impaired unless the tumour becomes necrotic and infected or occlude the urethral orifice, or metastasized. Hematocrit values are slightly lower than normal in less than 10% of the affected dogs, but no severe anaemia is found. The white cell count is higher than normal in about 30% of the cases; most dogs show a mild to moderate leukocytosis, probably caused by the inflammation of the tumour surface.

Microscopic Characteristics

Aspirates from TVTs are highly cellular and often bloody. Cytological examination reveals the typical round to slightly polyhedral cells. Individual neoplastic cells have a

round nucleus, fine to granular chromatin pattern, and often a single, prominent nucleolus. Mitotic figures are frequently observed. The cytoplasm is pale blue and moderately abundant, the nucleus to cytoplasmic ratio is large. The most prominent cytological feature of TVTs is the presence of distinct, clear, cytoplasmic vacuoles. TVT cells that lack cytoplasmic vacuoles may be easily confused with other round cell tumours. The morphological appearance and location of the tumour, however, are helpful in the diagnosis. A variety of inflammatory cells may be observed, especially in traumatized neoplasms.

Histologically, TVTs are made up of a homogenous tissue with a compact mass of cells that are histiocytic/mesenchymal in origin and the borders of which cannot easily be differentiated. Sometimes, however, they grow in rows, cords, or loose in a delicate stroma. As the tumour mass increases, the cells become tightly packed and irregular in shape and fibroblasts appear, perhaps an indication of the transformation of tumour cells. There is frequently an infiltration of lymphocytes, plasma cells and macrophages. TVTs should be differentiated from mastocytomas, histiocytomas or malignant lymphomas.

Diagnosis

Definitive diagnosis is based on physical examination and cytological findings typical of TVT in exfoliated cells obtained by swabs, fine needle aspirations or imprints of the tumours.

Treatment

Surgery, radiotherapy, immunotherapy, biotherapy and chemotherapy have been applied for treatment of TVT.

Surgery has been used extensively for the treatment of small, localized TVT, although the recurrence rate was as high as 50-68% in cases of large invasive tumours. Tumour cell transplantation into the surgical wound during operation is a source of recurrence. The use of electrocautery makes the operation easier and 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.

Transmissible venereal tumours are radiosensitive and orthovoltage as well as cobalt

have been used for this purpose. Dosage recommendations range from 1500 to 2500 rads, 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, specialized equipment and expenses. Therefore its use is recommended in cases where other treatments fail.

Immunotherapy and biotherapy have not been proven effective.

Chemotherapy has been shown to be the most effective and practical therapy. Antimitotic agents, such as cyclophosphamide, methotrexate, vincristine, vinblastine or doxorubicin, are the chemotherapeutic drugs for treating TVT, vincristine sulfate being the most frequently used drug.

Vincristine, is administered weekly at a dose of 0.5 to 0.7 mg/m^2 of body surface area or 0.025 mg/kg, IV. The involution of the lesions is gradual, although noticeable and significant at the beginning of the treatment. Complete remission usually takes 2 to 8 injections and occurs in more than 90% of the treated cases. A cure rate approaching 100% is achieved in cases treated in the initial stages of progression, especially in cases of less than 1 year duration, and independent of the presence or not of metastases. In cases of longer duration, longer periods of therapy are required, and the cure rate is lower.

Temporary side effects (partial anorexia, mild depression, fever, and vomition) are reported in less than 20% of the treated dogs, usually 1-2 days after vincristine administration. Vincristine, a cytostatic agent, can cause myelosuppression resulting in leukopenia. Paresis has also been described as a side effect due to peripheral neuropathy. A complete white blood cell count is, therefore, recommended prior to each administration. When the white blood cell count is below 4,000 mm^3 further administration should be delayed. The most frequent complication of vincristine treatment is the occurrence of local tissue lesions caused by extravasation of the drug during IV application resulting in the development of necrotic lesions with crusts.

Spermatogenesis can be temporarily or permanently altered by the administration of cytotoxic drugs. Drug-altered spermatogenesis may not return to normal for one or more spermatic cycles. Little information is available on the long-term effects of vincristine on male dog fertility. However, semen quality as assessed by volume and

sperm count of ejaculate; motility, viability and morphology of sperm deteriorates during the treatment and there is additive effect of duration of vincristine treatment on testicular functions. The semen quality may or may not be regained after vincristine treatment of male dogs and point out that the gonadal response to treatment varies among individuals.

Other chemotherapeutic agents indicated for TVT treatment include cyclophosphamide (5 mg/kg, PO, for 10 days as a single drug therapy or given in association with prednisolone, 3 mg/kg, for 5 days); also, weekly vinblastine (0.1 mg/kg, IV during 4 to 6 weeks), methotrexate (0.1 mg/kg, PO, every other day) or a combination of the 3 drugs. However, there is no apparent advantage in the combination of chemotherapy over using vincristine alone.

Resistant cases can be treated with doxorubicin (30 mg/m^2, IV, with 3 applications every 21 days). When total disappearance of the tumour cannot be achieved by chemotherapy, electro-cauterization or cryocauterization can be useful. After therapy, small remnant lesions can disappear spontaneously after 1 or 2 weeks. In cases that fail to resolve with chemotherapy, radiotherapy has been reported to yield good results.

Prognosis

The prognosis for TVTs is very good. Less than 5% of TVTs metastasize to other sites. Vincristine administration is the treatment of choice, with the majority of dogs being cured. Even in the case of metastasis, the cure rate for TVTs is over 90%. Dogs generally tolerate vincristine administration well; fewer than 15% of treated dogs experience drug-related side effects. For tumours that are resistant to vincristine, doxorubicin is the most effective chemotherapeutic agent. TVTs have also been shown to be very sensitive to radiation therapy.

Control

Control of TVT is difficult because stray dogs serve as a reservoir. Dog owners and breeders should carefully examine all males and females before mating and should also prevent mingling of valued dogs with strays. Careful examination of animals in breeding kennels before mating, with a view to not breeding from affected animals, will control the incidence of the disease. Where these factors have been in operation, the incidence of the disease has fallen and the disease is rare.