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Case report

Transmissible Extragenital Venereal Tumor in Impuberal Canine

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Abstract

Transmissible venereal tumor (TVT) is commonly observed in the external reproductive organs of sexually active canines. However, this tumor can unusually be identified in young dogs which have not reached reproductive capacity. In these latter animals, the tumor presentation is located in regions distant from the genitalia as integument and mucous membranes of body cavities. This study aimed to describe a case of TVT in a puppy dog. A seven month old female dog of the Labrador breed, had disseminated nodules in the skin and left conjunctival mucosa. Cytological examination of the proliferation was chosen, which led to the diagnosis of TVT. Since the dog showed no genital lesions, as she was impuberal, this was considered as an extragenital case. Chemotherapy protocol was established with vincristine sulfate, with complete remission of the lesion at the end of the fourth session. Later there was recurrence of the cutaneous TVT, being employed salvage therapy with vinblastine. However there was tumor resistance to such a drug. Surgical excision of the recurrent lesion was performed. It was demonstrated that TVT may also be adapted to other tissues and affect not only dogs at reproductive age, but also those at the pre-pubertal age.
Key Words: transmissible venereal tumor, sexual immaturity, alternative anatomical locations, dog.

Introduction

Transmissible venereal tumor (TVT) is a round cell neoplasm, common in domestic canids (2, 18). It presents a worldwide distribution, although it is more common in tropical and subtropical countries where canine population is not subject to strict epidemiological control (7, 19). The transmission is related to the stress inherent to the species intercourse, with the promotion of abrasion in the genital mucosa, which favors the establishment of viable neoplastic cells (20). Therefore, the tumor is usually observed in the external reproductive organs of sexually active animals (2, 18), being its genital presentation detected in approximately 67 % of TVT cases (20). There is no predilection for gender, but there is a higher incidence in not domiciled dogs, from two to five years old (1, 8, 9). However, there are descriptions, although unusual, of TVT in dogs aged less than twelve months and having not reached their reproductive capacity (1, 11). This situation is explained by the continued cohabitation and social interaction among mothers carrying the tumor and their offspring since there is predisposition for the neoplastic cells from the maternal genital TVT to contaminate the mucous membranes (nasal, oral, ocular, or anal) and tegument of the puppies. Thus, once the neoplasm is distant from the external genitalia, the TVT is characterized as extragenital (7).

In pediatric canines, tumor implantation can be widespread, with the possibility of aggressive clinical behavior (such as rapid neoplastic growth and metastasis) due to immunosuppression (11, 18, 20). The involvement

of multiple extragenital areas, besides compromising the tissues involved, can make a definitive diagnosis hard (7) due to the difficulty of distinction from other round cell tumors such as lymphoma, histiocytoma, mast cell tumors, amelanotic melanoma and undifferentiated carcinomas (12). However, cytological, histopathological and immunohistochemical features of TVT in non-genital areas, show similarity to the usual microscopic pattern of proliferation in the external genitalia (11, 12). When located in unusual areas, whether in body cavities, mucous membranes or the skin, TVT may prove sensitive or not to mono chemotherapy with vincristine sulfate (1, 11). Accordingly, the aim of this article is to report the existence of an extragenital TVT in a still pre-pubescent juvenile canine with the possible hypotheses for the acquisition of the neoplasm, clinical and microscopic characterization of the lesions, and multidisciplinary therapy employed.

Case report

A seven month old Labrador bitch, weighing 17 kg was examined for the main complaint about the presence of tumors under the skin, as well as the eye, with approximately thirty days evolution. The patient was raised indoors with no contacts. The vaccination protocol was outdated. In parallel, the animal was under hemoparasitic treatment. At physical evaluation the dog exhibited dyspnea, and emaciated and pale mucous membranes. There were several neoplastic nodules and disseminated tumors in the head (jaw regions, oral, frontal and parietal), ears, chest and abdominal area left and right sides (Figures 1A and B). Most of them showed a firm consistency, smooth shape, partial adherence to deep planes, sessile insertion base, with full surface and subcutaneous coverage. The conjunctival mucosa of the left lower eyelid presented a nodular mass (Figure 1B). There was a circumscribed and ulcerated lesion in the right forelimb (metacarpal region).

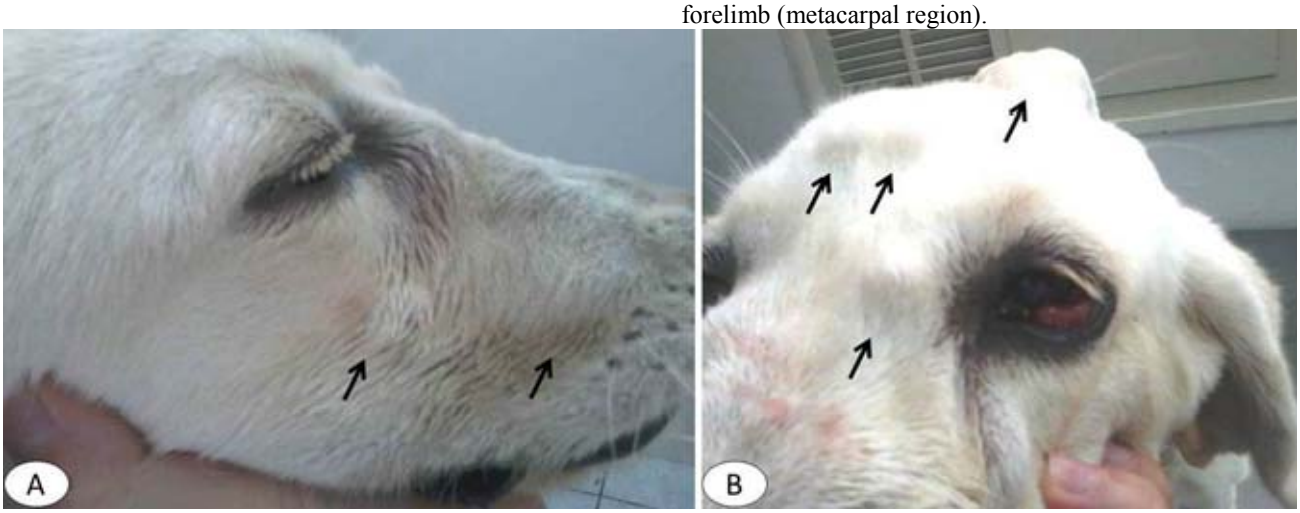

Figure 1. A and B. Multiple scattered nodules and tumors spread in the subcutaneous cephalic anatomic regions (arrows) and lower conjunctival mucosa close to the left eye.

Cytological examination (by the technique of fine needle aspiration of the conjunctival neoformation as well as in the subcutaneous area of the chest, and printing on the injury of the right forelimb) was performed. Microscopic inspection showed round cells with basophilic cytoplasm and distinct vacuoles. In most cells, the nucleus was eccentrically located with similar aspect to plasma cells. There were also mitotic figures (Figure 2). TVT diagnosis was established, presenting cytomorphological plasmacytoid pattern. It is noteworthy that the dog did not have lesions on the external genitalia, since it was impuberal. Thus, the case was considered as exclusively extragenital. Chemotherapy protocol was established with the use of vincristine sulfate intravenously at a dose of 0.75 mg/m² every seven days, a total of four applications. In the second administration, the proliferation had regressed considerably. At the time of the last session, there was complete remission of changes in the tegument and conjunctival mucosa. The dog showed no signs of dyspnea and her body condition improved. Throughout the treatment with vincristine sulfate side effects were not detected.

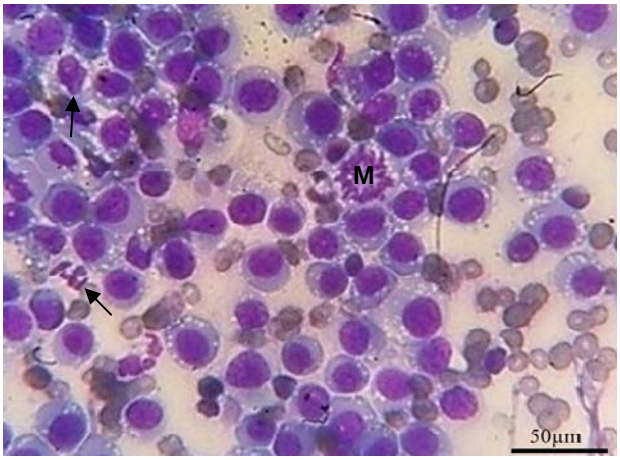

Figure 2. Photomicrograph of cytopathology elucidating characteristics of TVT cells with plasmacytoid pattern. M: mitotic figure; →: polymorphonuclear cell. Panoptic fast.

Thirty-five days elapsed when the owner returned with the animal, motivated by the emergence of a subcutaneous nodule, measuring 2,7x2,0x1,6 cm, located in the right costal wall. It was subjected to cytological examination and tumor recurrence was diagnosed. The use of vinblastine (2 mg/m², intravenously) was defined as rescue antineoplastic therapy. Seven days after the second dose, there was neogenesis, suggesting a framework for chemoresistance. Surgical excision of the lesion was the option of choice since it was restricted to a single anatomical site (Figure 3). The biopsy sample was fixed in 10% neutral-buffered formalin, routinely processed and embedded in paraffin. Five µm sections were stained with hematoxylin and eosin (HE) and scanned for cellular pattern. A neoplastic proliferation, expansive, infiltrative and covered by a fibrous capsule was detected. The cells were round and poorly differentiated, showing the core shifted to the periphery and a moderately abundant, eosinophilic and vacuolar cytoplasm. This morphological pattern was consistent with TVT (Figure 4), confirming the prior diagnosis established by cytopathology. The patient demonstrated adequate postoperative recovery. So far there have been no signs of further tumor recurrence.

Figure 3. Extragenital TVT in impuberal bitch, relapsing and chemo-resistent, in the pre-operative period (animal in the left lateral decumbency).

Discussion

TVT is a neoplasm that can primarily be transmitted by sexual intercourse, but also by means of licks and contact to mucous membranes. Generally, it affects dogs at about two to five years of age, mixed breed, with free access to the street, and sexually active (9, 14). The presented case differed from most in the literature as the animal was a seven month old puppy (and, therefore, still without reaching puberty or even sexual maturity), defined breed, without interaction with other canines or contact with the external environment. The translocation of extragenital TVT to alternative anatomical sites in juvenile dogs is possible due to social behavior and cohabitation between the carrier progenitor and the offspring (11). Thus, we have suggested a possible acquisition of the tumor during the passage of the canine through the birth canal (with the presence of intravaginal asymptomatic tumor). We also considered the post-natal interaction with the dam; it may well have been a straight deploying tumor through friction, scratch, licking, biting or sniffing. More remotely, it was hypothesized transplacental transmission in the case of a tumor in the uterine lumen. However, the assumptions mentioned above have not been confirmed due to the absence of concrete information about the condition of the mother's sanitary status.

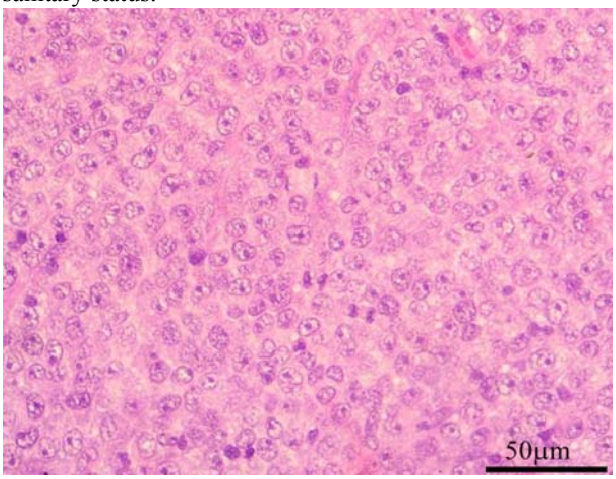

Figure 4. Histopathological pattern of extragenital TVT which underwent surgical excision. HE.

In most situations, the neoplastic mass is located in the external genitalia. However, TVT can arise in unusual areas such as the subcutaneous tissue (mainly in the head, neck , limbs and trunk), perineal and anal regions, ocular conjunctiva, third eyelid, pharynx and nasal and oral cavities, with no genital commitment (6, 7). Once in the integument, the proliferations may measure between two to thirteen centimeters in diameter, either alone or in a multiple way, being ulcerated or not (20). In the patient examined, the macroscopic skin lesions corroborated the literature findings. When the ocular TVT is initiated by implant, the new growth comes from the external structures, while in case of metastases, there is initial involvement of the vascular knit such as the iris, ciliary body, or choroid with intraocular development pattern (2). Thus, the reporting evidence reinforced that the ophthalmic neoplasm amounted to a primary extragenital translocation, since the TVT was restricted to the conjunctival mucosa. The verification of metastasis is rare and occurs mainly when the tumor persists for several months and when animals are immunocompromised or very young. The spread is directed to regional lymph nodes, lungs, nervous system and abdominal viscera. The immunocompetence tends to lead to tumor regression, unlike the cases of immune depression (5, 8). In the mentioned case, no image test was performed to investigate possible metastases, but the animal had dyspnea which was resolved after the treatment with

vincristine sulfate. This fact suggested probable lung metastases at the time of the initial approach. In the reported animal, the simultaneous involvement with hemoparasites may have favored the spread of tumor at distance, because of pancytopenia and bone marrow hypoplasia, leading to immunosuppressant conditions (13).

In general, TVT definitive diagnosis is based on history, physical examination and cytological findings (9, 16). The clinical information of the bitch under discussion did not lead to suspicion of TVT as the nodules and tumors were atypical, besides genital lesions were not present. Thus, the diagnosis was confirmed by microscopic examination of the samples obtained by fine needle aspiration and printing. The first of the above mentioned techniques is considered as an effective method in cases of skin proliferation (15). The cells found in the cytology followed plasmacytoid pattern, considered of high occurrence in cases of extra-genital TVT location (1). Such peculiar cytomorphology relates to higher rates of cell proliferation and increased expression of P-glycoprotein. The latter is present in the cell membrane and acts as a drug efflux pump, thus favoring the active expelling of the antineoplastic drug concentrated into the intracellular field, thus limiting the cytotoxic effects (10, 19). Being so, the microscopic plasmacytoid presentation described in this report, justified the drug resistance to a conventional therapeutic protocol.

Several treatments have been instituted for TVT control. Chemotherapy is widely used for being of low cost, practical and efficient (17). In our case, the treatment was chosen accordingly to the reported by other authors (3), which is the use of vincristine sulfate at a dose of 0.75 mg/m² intravenously, every seven days, from four to six weeks. After obtaining the complete regression of the tumor, it is suggested that two additional sessions must be made, in order to eliminate residual cancer cells (16). Although in the described case no side effects occurred, they may be observed in patients under treatment with vincristine sulfate, such as myelosuppression (mild to moderate), gastrointestinal disorder, peripheral neuropathy and dermal toxicity, mainly related to perivascular extravasation of the drug (3, 16). In the current situation, the option for salvage therapy with vinblastine instead of doxorubicin was made because the latter causes major side effects such as cardiac and hematological toxicity (17). However, this can induce a chemotherapeutic severe neutropenia (3). In the canine described, the discontinuation of such antineoplastic treatment was not associated with hematologic toxicity, but with the likely generation of tumor resistance mechanisms to multiple drugs.

Surgical resection is not indicated if the tumor is in the genitourinary area, once this procedure is extremely gory and at high risk of relapse (the infiltrative nature of the tumor and transplantation of tumor cells into the wound). The external urethral ostium may still be compromised by scar deformities. However, this therapeutic modality is recommended in cases of lesions remaining from chemotherapy which are of small size, alone and in easily accessible locations (5, 8). It is also recommended surgical removal followed by crionecrosis, aiming the destruction of remaining cells by the thermal process and consequently reducing recurrence rates (8). In the present case, because of the macroscopic residual dermal neoformation, the operative technique was justified. In cases of TVT affecting females, ovariossalpingohysterectomy is recommended because it was proved the relationship between estrogen and increased vaginal tumor growth (4). In this patient, sterilization was not an option due to the absence of tumor in the external genitalia. Moreover, even if this location presented neoplasia, the reproductive condition of the bitch probably would not influence the tumor progress due to the ovarian immaturity in terms of hormone secretion.

TVT (although detected in most cases in the genital male and female canine species) can also adapt, grow and spread through various tissues differently from those related to the reproductive system. Furthermore, not only it affects the sexually active animals, but also those who are still in the impuberal phase. Thus, one should not rule out the possibility of TVT (even with extragenital presentation) until undergoing a cytological and/or histological exam. Although mono chemotherapy with vincristine sulfate is classically employed in most situations, it may be necessary to adopt other anticancer drugs in cases of tumor recurrence or even the introduction of other forms of treatment.

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