

Atypical Transmissible Venereal Tumor in Dogs

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ABSTRACT

Background: The Transmissible Venereal Tumor (TVT), classified as a round cell tumor, is considered one of the oldest existing tumors. It affects dogs all over the world and has a contagious characteristic. Despite the good response to clinical treatment in most cases, it can sometimes have non-classical presentations and even different behavior. Thus, the present study aims to report 3 cases of atypical TVT treated at the Veterinary Medical Teaching Hospital of the State University of Maringá (UEM) in Umuarama, Paraná, aiming to describe the epidemiology and clinical-pathological aspects, focusing on the diagnostic method used, the treatment of choice and the clinical follow-up of each case.

Cases: Case records of 3 intact male mongrel dogs with atypical Transmissible Venereal Tumor (*case 1*: intranasal; *case 2*: intra-abdominal and *case 3*: cutaneous with lymph node metastasis) were reviewed regarding history, clinical signs, duration of clinical signs, examination findings, results and findings of complementary exams (hematological, biochemical, radiographic, ultrasonographic and cytological), treatment, follow-up and final result. *Case 1*: had an ulcerated mass in the nasal plane causing significant airway obstruction and respiratory difficulty. *Case 2*: had a lesion in a typical location (penile mucosa in the glans area) but with a large intra-abdominal mass in the lumbar paravertebral region, causing compression of important structures. *Case 3*: on the other hand, had cutaneous TVT with several ulcerated plaque lesions all over the skin, in addition to popliteal lymph node enlargement due to metastasis later confirmed by microscopy. All dogs reported were mixed breed, intact males with free access to the street. Despite the fact that each patient had their own anatomical tumor characteristics, they were all diagnosed through cytological examination and all classified as lymphocytic TVT. The standard treatment for this neoplasm was instituted; the chosen chemotherapy was vincristine sulfate at a dose of 0.75 mg/m² intravenously every 7 days for 5-7 weeks. In addition, all 3 animals needed supportive treatment due to anorexia, bacterial contamination secondary to injuries, dehydration and pain.

Discussion: Usually, TVT is not considered malignant, not causing metastasis, however it is now known that its behavior has changed a lot and more and more cases of metastatic or highly infiltrative TVT have been reported. The 3 cases presented in this report had epidemiological characteristics as mentioned in the literature, but the location, macroscopic and radiographic characteristics are uncommon for this neoplasm, that is, with an atypical tumor presentation. This demonstrates the importance of a good clinical evaluation and, especially, of the cytological exam, which was essential for the definitive diagnosis for the three cases presented. It is speculated that more “aggressive” cases of TVT may be correlated with the plasmacytic cytological type, however none of the patients described here had this cytological presentation. Thus, the clinician must be aware of the risk factors associated with this neoplasia, because even in non-classical presentations, the lymphocytic cell morphological characteristic was present and the patients responded well to the classic treatment, not requiring a change in chemotherapy protocols, however a special attention must be paid to the particularities involved in each presentation of the same tumor in different patients.

Keywords: TVT, canine, neoplasm, metastasis, cytology.

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INTRODUCTION

Transmissible Venereal Tumor (TVT) is a round cell tumor that affects dogs all over the world and presents a contagious characteristic, being acquired through the contact of affected mucous membranes with cancer cells, mainly during intercourse [4,7,10,18,19,21].

Macroscopically, it is characterized by an invasive, irregular lesion with an increased number of blood vessels on the surface [10], which may present ulcers and incessant bleeding [18]. Regarding its microscopy, there are 3 subtypes: plasmacytic, lymphocytic and intermediate [3].

The clinical presentation of the patient varies according to the anatomical location of the tumor. In the most common region (genital) animals may present a visible mass, intense odor, ulceration, necrosis, serosanguineous secretion and dysuria [6,18].

The definitive diagnosis is based on cytological analysis, histopathology, electron microscopy or immunohistochemistry [4,9,20].

Regarding treatment, there are several modalities that can be performed, such as radiotherapy, surgery, immunotherapy and chemotherapy [4,6,8,9,12,13,16]. The prognosis is considered good, as, in general, there is complete regression of the tumor by chemotherapy [8,18].

The aim of this article is to report 3 cases of atypical transmissible venereal tumor in dogs treated at the Small Animal Medical Clinic - Veterinary Medical Teaching Hospital of the State University of Maringá (UEM), describing the epidemiology and clinical-pathological aspects of each case, focusing on the diagnostic method used, the treatment of choice and progression of each condition.

CASES

The records of 3 cases of dogs with atypical Transmissible Venereal Tumor (*case 1*: intranasal; *case 2*: intra-abdominal and *case 3*: cutaneous with lymph node metastasis) have been revised. Data and their analysis include history (from August 2017 to May 2018), clinical signs, duration of clinical signs, physical examination findings, results and findings of complementary exams (hematological, biochemical, radiographic, ultrasound and cytological), treatment, follow-up and outcome/final result. Blood count was performed in all cases, whereas serum biochemical

analyzes (urea, creatinine, alanine aminotransferase, alkaline phosphatase and albumin) were performed only in case 2.

Radiographic examination of the cranium (laterolateral projection) and thoracic region (laterolateral and ventrodorsal projections) was performed in case 1 and of the thoracic and abdominal regions (laterolateral and ventrodorsal projections) in cases 2 and 3, through physical restraint. In addition, complete abdominal ultrasound examination was performed in cases 2 and 3. Diagnosis was based on epidemiology and macroscopic and cytological examinations of the lesions. Cytology was performed in all animals, from samples of nodules of the snout (case 1), nonspecific abdominal mass (case 2) and cutaneous nodules in the dorsal region, ventral portion of the neck, penile foreskin and left popliteal lymph node (case 3); all collected by fine needle aspiration (FNA) puncture using a 22G needle coupled to a 5 mL syringe, in case 2 the ultrasound guided technique was performed. Slides were stained with Romanowsky stain¹ [Fast Panoptic[®]] and analyzed using light microscopy² [Nikon Eclipse E200[®]].

Treatment of the 3 cases was standard; the chosen chemotherapy was vincristine sulfate³ [Tecnocris[®] 0.75 mg/m² intravenously in bolus every 7 days for 5-7 weeks]. In addition, all 3 animals needed supportive treatment due to anorexia, bacterial contamination secondary to injuries, dehydration and pain. Cases 1 and 2 were hospitalized for antimicrobial therapy, fluid therapy, analgesia and anti-inflammatory therapy, and in case 1, specifically, daily dressings were also applied to the lesion. Case 3 was able to receive support at home. The follow-up of all cases was carried out with returns, exams and telephone communication with the owners.

All 3 dogs reported were intact male mongrel dogs. The mean age was 4 years \pm 2.6 years (2 to 7 years) and their mean body weight was 7.83 kg \pm 5.38 kg (3.5 to 13.85 kg). All animals had free access to the street and contact with stray dogs. All cases had chronic manifestations (mean of 3 months).

Case 1. Dog had an increase in volume / ulcerated mass in the nasal region measuring 10 x 6 x 2.5 cm (Figure 1), which drained a foul-smelling blood purulent secretion. The mass had a proliferative and friable aspect (cauliflower), it was fistulated, with necrotic areas and compromised part of the nasal bone and left



Figure 1. Photographic image showing the macroscopic aspect of the lesion [case 1]. An ulcerated lesion with raised borders, bloody and with necrotic areas invading the nasal sinus and medial corner of the left eye can be seen.

orbital region. Occasionally, it caused breathing difficulties, constant discomfort and apathy to the animal.

Case 2. Dog had masses in the paravertebral lumbar, inguinal, intra-abdominal and penile mucosa in the glans area (1.5 cm). The lumbar mass was soft and slightly reducible, while the lesion on the glans had a vegetating aspect. Regarding clinical signs, he presented apathy, weight loss, dehydration, hyporexia, oligodipsia, dyschezia and tenesmus, sometimes with blackened stools (melena).

Case 3. The patient (Figure 2), on the other hand, had several cutaneous and subcutaneous nodules of firm consistency and varying sizes, spread throughout the body, mostly ulcerated. Ulcerated lesions, as in case 1, were prominent with raised borders, necrotic areas and drained purulent blood secretion. Furthermore, the animal had an increase in volume/mass in the submandibular lymph nodes (left and right) and left popliteus. As a clinical sign, it expressed pain on abdominal palpation (epigastric, mesogastric and hypogastric regions) and apathy.

Among the 3 cases mentioned, the only common clinical sign was apathy. In addition, on admission, anemia was observed in the blood count of cases 1 and 3. Case 1 presented a regenerative hypochromic microcytic anemia (red blood cells 4.1 million/ μL , hematocrit 23%, mean corpuscular volume 56.1 fL and mean corpuscular hemoglobin concentration 30.9 g/dL, with presence of anisocytosis, polychromasia and Howell-Jolly corpuscle) and, in case 3, normochromic regenerative normocytic anemia (red blood cells 4.36million/ μL , hematocrit 28.7%, hemoglobin 9.5g/dL, mean corpuscular volume 65.8 fL and mean corpuscular hemoglobin concentration 33.10 g/dL, with presence of anisocytosis, polychromasia and metarubrocytes 2%). Only the animal in case 1 had thrombocytopenia (144,000 platelets/ μL and macroplatelets). Furthermore, in relation to white blood cells, patient in case 2 had leukocytosis (18,330/ μL) due to neutrophilia (15,214/ μL), with a shift to the left (bands 733/ μL) and animal 3 had lymphopenia (249 μL).



Figure 2. Photographic image of a dog with cutaneous TVT [case 3]. A- Side view & B- Front view. In both photos, the presence of large ulcerated cutaneous nodules can be seen, located in the cervical and thoracic regions.

Serum biochemical analyzes (urea, creatinine, alanine aminotransferase, alkaline phosphatase and albumin) performed in case 2 showed no significant changes. In all cases, radiographic examination was performed to assess the masses and search for metastases. In case 1, no thoracic alteration was found, however a severe increase in soft tissue radiopacity of the nasal cavities and paranasal sinuses and a severe increase in soft tissue volume in the incisor, nasal, maxillary and frontal bone region were detected, measuring approximately 10.74 x 5.24 cm with heterogeneous radiopacity, cavity areas and mineralization points. Severe bone lysis of the nasal conchae, vomeronasal bone, with bilateral destruction of incisor, nasal, maxillary and frontal bones. Bone lysis of the cleft palate, of the alveolus of the upper right and left canine teeth, and of the upper left first, second and third premolars (Figure 3). According to the report, the skull radiographic image was compatible with osteolytic neoplasm in the nasal/frontal plane associated with bilateral sinusitis.

In case 2, no thoracic alterations were found, however, on the abdominal radiography (Figure 4), the presence of a mass measuring 11.42 x 5.58 cm was found, being slightly radiopaque compared to the adjacent abdominal organs. In the animal of the third case, there were no thoracic and abdominal changes.

In the second and third cases, ultrasound examination was necessary. In case 2, a mass was observed in the hypogastric region, close to the urinary vesicle, in the topographical region of the prostate. It had a heterogeneous appearance, with cystic areas, irregular edges and a length of approximately 12 cm. The mass compressed the right ureter, leading to hydronephrosis with dilatation of the right renal pelvis by 1.3 cm. The intestinal loops were cranially displaced, as were the spleen and kidneys. A homogeneous, hypoechoic rounded structure was also observed in the topography of the inguinal lymph node, measuring around 4.47 x 3 cm. In case 3, hepatomegaly, hepatic congestion, hyperechogenic liver, diminished and heterogeneous right testis were detected.

In the cytological examination (Figure 5), in all cases, a moderate amount of red blood cells, intact and degenerated neutrophils and small lymphocytes was observed. High cellularity, with round cells distributed in a monolayer, with moderate to high nucleus/cytoplasm ratio and moderate anisocytosis. Basophilic cytoplasm, sometimes vacuolated, eccentric nucleus with loose

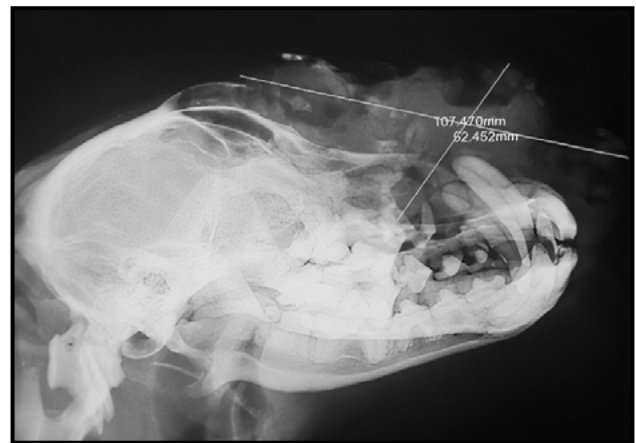


Figure 3. Radiographic image of the skull of a dog with intranasal TVT [case 1], showing osteolytic neoplastic infiltration in the nasal/frontal plane.

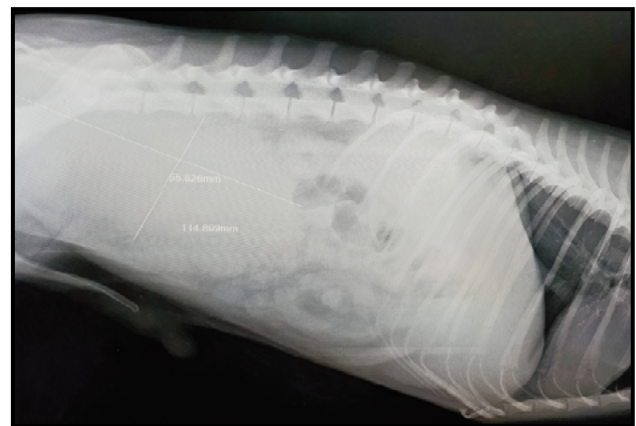


Figure 4. Thoraco-abdominal radiographic image, in lateral/lateral projection of a dog with intra-abdominal TVT [case 2], showing a mass of 11.42 x 5.58 cm.

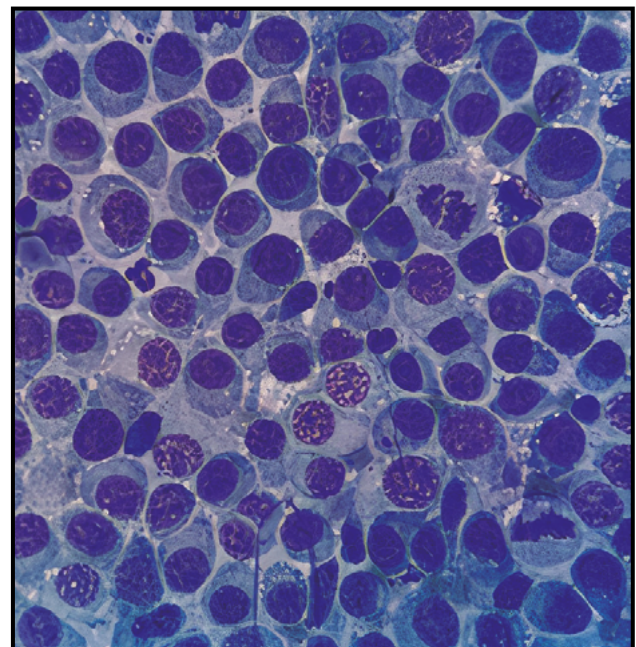


Figure 5. Photographic image of a cytological slide of TVT of the lymphocytic subtype.

chromatin, evident nucleolus and large number of mitotic figures, confirming the diagnosis of transmissible venereal tumor. Furthermore, the cell classification in all cases was of the lymphocytic subtype.

In all cases, the animals responded well to chemotherapy treatment, with complete tumor remission. In case 1, one week after the first chemotherapy session there was already a significant reduction in mass size and secretion, from 10 x 6 x 2.5 cm to 3 x 2 x 1 cm (Figure 6), and in the second session there was a reduction in respiratory difficulty and, in the fourth, almost total mass reduction.

In the second case, there was also a significant reduction in mass (10 x 5.1 cm) after the first treatment session, in addition, the abdominal organs remained dorsocranially dislocated and, on abdominal ultrasound, there was a decrease in renal pelvis dilatation (0.72 cm) and the kidney was in its usual topography. In the fourth session, there was no dilation of the renal pelvis, and there was a decrease in the mass size (6.04 x 2 cm), in addition, the penile mass disappeared. After 42 days of treatment, the ultrasound examination revealed that the abdominal organs were in the usual topography and the mass reduced in size to 5.39 x 1.7 cm. In the third case (Figure 7), the skin nodules regressed during the chemotherapy sessions, while the lymph nodes reduced in size in the second session.

DISCUSSION

Despite being a disease reported around the world, it is mainly identified in tropical and subtropical urban areas of developing countries, where there is an environment with a large population of stray dogs

without mating control; pattern followed by the three reported cases [4,8].

This occurs since TVT is transmitted through contact between mucous membranes, especially during intercourse, that is, mainly affecting the genitals. However, it can also be transmitted by licking, scratching, biting and the act of sniffing, affecting primarily and less frequently other places such as the nasal cavity, mouth and rectum; possibly as occurred in the first reported case (nasal TVT). Even more rarely, it can affect the lips, eyes, conjunctiva, auditory pinna, musculature, cutaneous and subcutaneous regions; as in the third reported case of cutaneous TVT [4,14,17].

Usually, TVT is not malignant, not being able to metastasize, but there are rarely reports (less than 5% of cases) that it can occur in regional lymph nodes, liver, lung, kidney, spleen and brain; affecting only immunocompromised animals or puppies [6,7,10,14]. Thus, the second case of abdominal TVT report occurred through metastasis, as well as the third case, where, in addition to cutaneous TVT, the animal presented metastasis in lymph nodes.

One hypothesis to explain how the tumor invades the organism without causing immunological alarms is that it causes the suppression of the host's DLA (Dog Leukocyte Antigen) activity through the secretion of inhibitory factors (TGF- β 1 and IL-6). This is an evolutionary adaptation mechanism that rarely results in host death, ensuring tumor transmission during the subsequent reproductive cycle [11,21]. However, it cannot be affirmed that in the reported cases TVT has spread through these mechanisms since



Figure 6. Photographic image of a dog with TVT in the nasal region [case 1]. A- Before the first chemotherapy session. B- One week after the first chemotherapy session. C- One week after the fourth chemotherapy session.

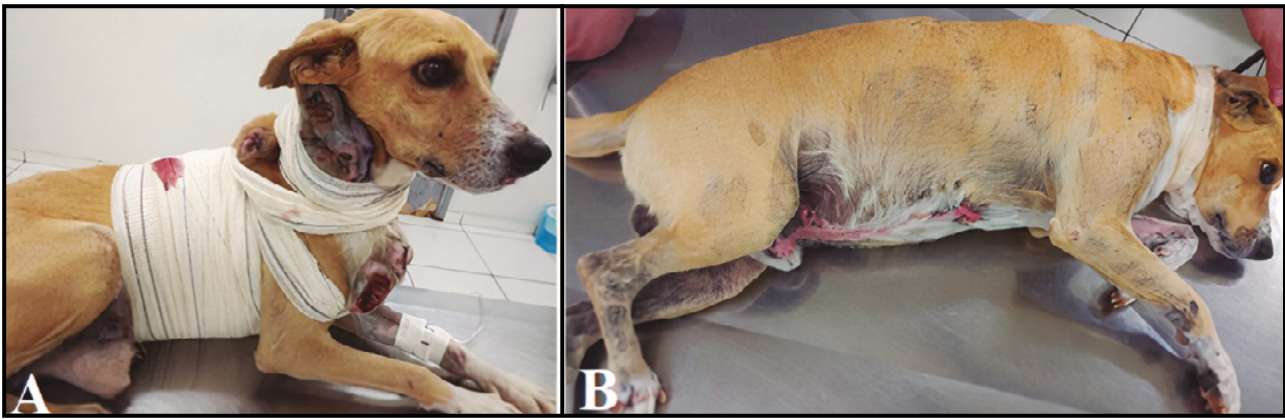


Figure 7. Photographic image of a dog with metastatic cutaneous TVT in lymph nodes [case 3]. A- Patient before the first chemotherapy session. B- Complete remission of the lesions is noted after the end of seven chemotherapy sessions with vincristine.

these interleukins are not frequently dosed in hospital routine except in experimental animals.

Regarding macroscopy, the literature describes TVT as a tumor formed by one or more irregularly shaped, friable, reddish nodules, which may present ulcerations. With a vegetative, sessile or pedunculated aspect, reaching up to 15 cm in an advanced stage [10,13,15,18]. The only formations that differed from the above description were some cutaneous and subcutaneous nodules from the third case that had a firm consistency and were not ulcerated.

The macroscopy of the tumor, as well as its location, influence the form of clinical presentation [6]. Despite this, there are rarely reports of severe cases of TVT, with large facial deformity and radiographic characteristic of osteolytic neoplasia, as in the first case [18]. Also describes cases with osteolysis of nasal bones [5]. Furthermore, other signs presented by these 3 dogs were reported as melena, hydronephrosis with dilation of the renal pelvis and displacement of organs as in the second case; large and varied cutaneous nodules, hepatomegaly, hepatic congestion and lymph node metastasis, as in the third case, are not commonly observed in routine.

In the blood count, the alterations are usually influenced by various factors, such as negligence in health care by the owners and the location of the tumors. Normocytic normochromic or hypochromic anemia, neutrophilic leukocytosis, and thrombocytopenia are commonly reported; similar to what was found in these cases [18].

In clinical practice, the diagnosis of extragenital TVT can be challenging. It is accurately diagnosed, differentiating it from other round cell tumors, using

complementary techniques such as cytology, histopathology or even immunohistochemistry [1,2,4,6,9], in this report the fine needle aspiration cytology technique was used in the 3 cases.

Through cytological examination, TVTs can be subclassified as lymphocytic, plasmacytic or compound. The plasmacytic subtype is usually found in metastatic TVTs, contrary to what was seen in cases 2 and 3 of the present report; since all cases were lymphocytic subtype, which is more frequently reported and with a good prognosis [3]. Finally, there are several treatment modalities that can be performed, however chemotherapy with vincristine as a single agent has been shown to be effective leading to complete tumor remission, as seen in the cases described where, despite being locally invasive, the 3 animals had a good response to instituted therapy.

The 3 cases presented have epidemiological characteristics as mentioned in the literature, however with atypical tumor location and presentation. Therefore, the clinician must be aware of the risk factors associated with this neoplasm, even in tumors with non-classical presentations. Furthermore, it is worth emphasizing the importance of cytological examination for the diagnosis and therapeutic definition of each case, as it is a simple, fast and inexpensive method to diagnose TVT.

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