



CASE REPORT

Disseminated metastatic transmissible venereal tumour in a bitch

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Özet

Kose AM, Cizmeci SU, Aydin I, Dinc DA, Maden M, Kanat O. Bir köpekte yaygın metastazlı transmissible venereal tümör. *Eurasian J Vet Sci*, 2013, 29, 1, 53-57

Bu vakanın materyalini doğum sonrası üç aydır devam eden kanlı vaginal akıntısı olan 4 yaşlı Sibiryan Husky ırkı dişi bir köpek oluşturdu. Yapılan fiziksel muayenede deri altında birçok noktada çeşitli büyüklükte kitlelerin olduğu, kanlı vajinal akıntının bulunduğu, vulvanın ödemli olduğu ve üzerinde dokunulduğunda kolayca kanayan karnabahar görünümü frajil tümöral kitlelerin bulunduğu belirlendi. Vajinadaki tümöral kitlelerden hazırlanan smear preparatlarının sitolojik incelemesinde yuvarlak hiperkromik çekirdek ve çekirdekçiği bulunan ince stoplazmalı, eozinofilik vakuollü yuvarlak, oval ya da polihedral görünümü tipik transmissible venereal tümör hücrelerine rastlandı. Ultrasonografik muayenede ise karaciğer, dalak ve sol böbreğin ekojenitelerinde değişiklik olduğu, karaciğer ve dalağın büyüdüğü ayrıca karaciğer üzerinde çok sayıda dalakta ise bir adet kitle olduğu belirlendi. Yapılan klinik, labaratuvar, radyografik ve ultrasonografik muayeneler sonucunda vakada yaygın metastazlı transmissible venereal tümör (TVT) teşhis edildi. Vakanın prognozunun kötü olması nedeniyle hasta uyutuldu. Nekropsi sırasında deri, derialtı, memelerin etrafı, son kosta üzerie, abdomen, akciğer, karaciğer ve dalakta matastazik kitleler belirlendi. Genellikle benign karakterde olan ve metastazlara nadir rastlanılan TVT olgusu, bu vakada deri, derialtı dokular, meme, karaciğer, dalak ve akciğerde metastazlara yol açıp malign karaktere döndüğü belirlendi. Sonuç olarak TVT'li köpeklerde metastaz varlığının araştırılması için dikkatli bir sistematik muayene yapılmalıdır.

Anahtar kelimeler: TVT, metastaz, dişi köpek

Abstract

Kose AM, Cizmeci SU, Aydin I, Dinc DA, Maden M, Kanat O. Disseminated metastatic transmissible venereal tumour in a bitch. *Eurasian J Vet Sci*, 2013, 29, 1, 53-57

The material of this case is a 4-years-old Siberian Husky bitch with 3 months of continuous postpartum bloody vaginal discharge complaints. There were subcutaneous masses in various sizes in many points, vaginal bloody discharge, edematous vulva with fragile and easily bleeding on touch, cauliflower looking tumoral masses as noticed during physical examination. Typical transmissible venereal tumor (TVT) cells, shaped round, ovoid or polyhedral with eosinophylic vacuole, thin cytoplasm, round hyperchromatic nucleus and nucleolus were observed on cytological examination of smears prepared from tumoral masses in vagina. There were changes in echogenities of liver, spleen and left kidney, hepatomegaly, splenomegaly and besides many mass formations in liver and one in spleen on ultrasonographic examinations. Disseminated metastasized TVT was diagnosed in the bitch depending on clinical, laboratory, radiographic and ultrasonographic examinations. Prognosis of the case was bad thus the patient was euthanized. Metastasized masses were observed during necropsy in skin, subcutaneous and around the udders, on the last rib, in abdomen, lung, liver and spleen. It was observed that TVT case, which is benign usually and metastatic rarely, turned malign and metastasized to skin, subcutaneous tissue, udders, liver, spleen and lung. In conclusion, a careful systemic examination and inquiring the presence of metastasis should be considered in dogs with TVT.

Keywords: TVT, metastasis, bitch



Transmissible venereal tumor (TVT) is located in external genital organs of dogs and usually transmitted by coitus. TVT, also known as infectious sarcoma, venereal granuloma, transmissible lymphosarcoma or sticker tumor, is a benign reticuloendothelial tumor that affects particularly mucosa of external genital organs and rarely internal genital organs in dogs of both genders (Chu et al 2001, Stettner et al 2005, Murgia et al 2006, Purohit 2009, Cizmeci et al 2012). TVT cases are particularly observed in dogs with high sexual activity (Nak et al 2005). Disease is more common in 2-8 years aged animals (80%) and more frequent particularly in female dogs (64.5%) than in male dogs (35.5%) (Eze et al 2007, Aydin et al 2009) and there is no racial predisposition (Gulbahar and Haziroglu 1995).

TVT is the first tumor reported as contagious between animals (Nak 2001). Although TVT is usually transmitted by coitus, it also can be transmitted by licking, sniffing, biting, and scrabbling of the tumor affected area or through damaged skin and mucosa (Stettner et al 2005). Transmission is directly through transplantation of live tumor cells. However, frozen, heat or glycerin treated tumoral cells or filtrates without cell do not form tumor (Murgia et al 2006). Tumor is usually located in posterior vagina and frequently in vestibulovaginal junction in bitches and it is observed as prolapsed out of vulva of bitches in most cases (Nak et al 2005, Purohit 2009, Stockmann et al 2011). Besides external genital organs, tumor can also be found in bucca, nasal and anal mucosa, conjunctiva and skin, as well (Eze et al 2007). Tumoral cells are big, round, polygonal or oval as observed in histopathological inspection. There are vacuoles and big nucleuses in those cells. A dark colored nucleolus is placed in nucleus. Its cytoplasm is slightly eosinophilic. Mitotic activities of cells are increased and a thin connective tissue rich in blood vessels observed in tumoral mass (Nak 2001, Stockmann et al 2011).

There were local invasion cases in 40% of dogs with TVT while 5-7% of those were metastatic (Kahn 2005, Purohit 2009). In fact, metastasis is mechanical extension of tumoral growth or automatical or mechanical transportation of tumor located on external genital organs to cervix, uterus and oviduct in most cases (Das and Das 2000). Metastasis in TVT cases may occur in inguinal and external iliac lymph nodes and in skin as well. Although metastasis is not common, it is reported to spread into regional lymph nodes, tonsils, eye, brain, adenohypophysis, nose, liver, spleen, lung, bone, kidney and other parts (Kahn 2005). Tumor grows rapidly and can metastasize frequently to skin, inguinal lymph nodes and other mucous membranes and rarely to other organs in immunosuppressed adult dogs and puppies (Perez et al 1998, Purohit 2009).

TVT can be diagnosed by clinical and histopathological examinations. Besides, immunohistochemical techniques, chromosomal analysis and tumor transplantation trials may be used for diagnosis (Nak 2001). Many options such as surgery, immunotherapy, biotherapy, radiotherapy, and chemotherapy are available for the treatment. Chemotherapy is most easy and efficient way of treatment (Eze et al 2007).

The material of this case is a 4-years-old Siberian Husky bitch with 3 months of continuous postpartum bloody vaginal discharge complaints with brought to Veterinary Obstetrics and Gynecology Clinics of University of Selcuk. There were subcutaneous masses in various sizes in many points (Figure 1), bloody vaginal discharge, edematous vulva with fragile and easily bleeding, cauliflower looking tumoral masses on touch as notices during physical examination (Figure 2). Typical TVT cells were observed with big nucleus and vacuole during vaginal cytological examination (Figure 3). Hematological (Medonic, CA530®-Thor-haemocell counter) and venous blood gas (GEM® Premier 3000) parameters, results of biochemistry (BT 3000 plus®) of the bitch were shown in Table 1. Laboratory results indicated that there were leucocytosis, hemoconcentration, micrositic hypochromic regenerative anemia, hypernatremia and increase in serum AST, ALT, ALP and CK concentrations (Table 1). Hepatomegaly, splenomegaly, many masses in liver (Figure 4) and one mass in spleen were observed in transabdominal ultrasonographic (Mindray DC-6Vet) examination. There were changes in echogenity of liver, spleen and left kidney. There was no metastasis finding in lungs during direct ventro-dorsal radiographic examination (Imago Pratic 1 Top 1006®). Prognosis of the bitch was negative, thus it was euthanized by IV administration of 50 mg/kg thiopental sodium (Pental® Sodyum 1g, I.E Ulagay, Istanbul). Many masses were observed as big as 0.5-3 cm in diameter in skin, subcutaneous tissue and around the udders during necropsy. A mass with 1 cm in diameter was observed on the most caudal rib and another mass with 5-6 cm in diameter was observed on abdomen. Liver was fairly hypertrophic, deformed and there were many white, cauliflower looking, exuberant masses on it (Figure 5a). There was a mass with 3 cm diameter on spleen and thus it was deformed (Figure 6a). A mass with 1 cm diameter was observed in medial lobe of the lung (Figure 7a). The case was diagnosed as TVT with diffuse metastasis depending on clinical (Figure 1 and Figure 2), radiography, ultrasonography (Figure 4) and histopathology (Figure 5b, 6b, 7b) results.

TVT generally occurs in animals aged 2-8 years and it is more common between female dogs than male dogs (Eze et al 2007, Aydin et al 2009, Oruc et al 2011). The presented case of a 4 years aged bitch was TVT with a diffuse metastasis in many organs. It was observed that the tumor was located in vulva and expanded through vagina, with typical cauliflower looking, fragile and easily bleeding on touch due to increased vascularization.

The typical TVT cells (big, round, polygonal or oval with slight eosinophilic cytoplasm, vacuoles and big nucleuses which have big and dark hyperchromatic nucleoluses in their center) (Salt et al 2005, Stockmann et al 2011) were observed on cytological examination of smears prepared from this case (Figure 3). Initially TVT grows rapidly and gets stabilized for a certain time, regresses spontaneously few months later. It is reported that tumoral regression is related to lymphocytes in increased number of tumoral infiltrations which is characterized by apoptotic tumoral cells and fibrosis (Gonzalez et al 2000). Regression in TVT is not always spontaneous due to increased mitotic activity and minimum lymphocyte count (Park et





Figure 1. Subcutaneous masses in the bitch (arrows).



Figure 2. Appearance of vulva in the bitch with TVT.

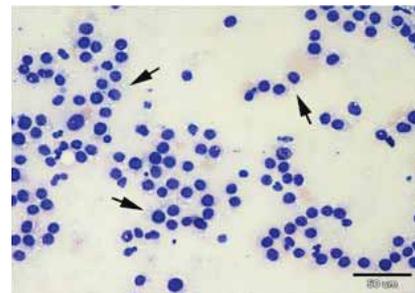


Figure 3. Vaginal smear obtained from the bitch with TVT. Typically round to polyhedral tumour cells, hyperchromatism and cytoplasm with punctate vacuoles (arrows) (May-Grunwald Giemsa stain).

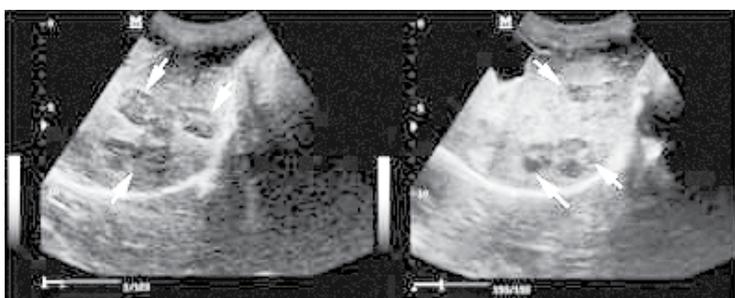


Figure 4. Many masses in ultrasonographic examination of liver (arrows).

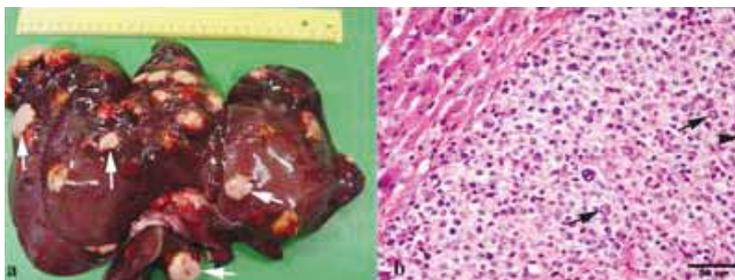


Figure 5. a- Cauliflower-looking masses on liver (arrows), b- Liver; Pleomorphic neoplastic cells (arrows) separated by scanty stroma (arrow head) (H&E stain).

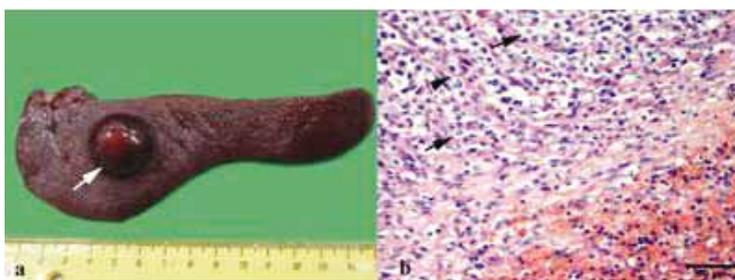


Figure 6. a- A mass on spleen (arrow), b- Spleen; TVT cells, arranged in loose sheets of round to polyhedral (arrows) divided by thin connective tissue stroma (arrow head) (H&E stain).

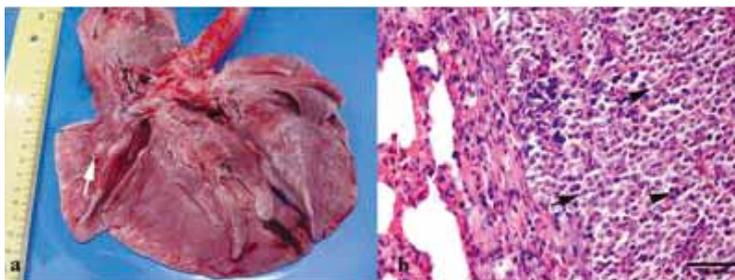


Figure 7. a- A mass in medial lobe of the lung (arrow), b- Lung; TVT cells (arrows) and mitotic figure (arrow head) (H&E stain).



Table 1. Laboratory parameters of the bitch.

Blood serum chemistry		Haematology		Venous blood gases	
Values (Ref values)	Values	Values (Ref values)	Values	Values (Ref values)	Values
AST IU/L (10-88)	154	WBC 10 ⁹ /L (5-14)	20.7	pH (7.35-7.45)	7.43
ALP IU/L (20-150)	141	RBC 10 ¹² /L (4.5-7.9)	8.95	pCO ₂ mm/Hg (35-45)	28.0
ALT IU/L (10-88)	139	HBG g/L (120-180)	164	pO ₂ mm/Hg (35-45)	43.3
CK IU/L (20-200)	829	HCT % (0.40-0.57)	0.63	Na mmol/L (140-155)	155
ALB g/L (23-38)	28.7	MCV (fL) (66-77)	70.2	K mmol/L (3.5-5.0)	3.43
TP g/L (54-77)	62.9	MCH pg (21-26)	18.3	HCO ₃ mmol/L (18-25)	20.4
LIP U/L (25-750)	712	MCHC g/dL (32-36)	26.1	O ₂ sat % (40-80)	81.4
TB µmol/L (1.7-10)	1.71	RDW % (12-16)	18.5		
C µmol/L (44-132)	45.0	PLT 10 ⁹ /L (211-621)	487		
BUN mmol/L (4.3-8.9)	4.4				

WBC: White Blood Cell, RBC: Red Blood Cell, HGB: Hemoglobin, HCT: Hemocrit, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, MCHC: Mean Corpuscular Hemoglobin Concentration, RDW: Red Blood Cell Distribution, PLT: Platelet. pCO₂: Carbon Dioxide Partial Pressure, pO₂: Oxygen Partial Pressure, Na: Sodium, K: Potassium, HCO₃: Bicarbonate, O₂ sat: Oxygen Saturation. AST: Aspartate Aminotransferase, ALP: Alkaline Phosphatase, ALT: Alanine Aminotransferase, CK: Creatine kinase, ALB: Albumin, TP: Total Protein, LIP: Lipase, TB: Total Bilirubin, C: Creatinine, BUN: Blood Urea Nitrogen.

al 2006). Depending on anamnesis, tumor had predisposition for growing and the masses did not regress in the case presented.

Microcytic hypochromic regenerative anemia was linked to hemorrhagic anemia due to tumoral bleeding while haemoconcentration and hypernatremia were linked to dehydration and leucocytosis was linked to infection in tumoral tissue and its periphery, depending on laboratory results of the case. Increased serum AST, ALT and ALP activities (Table 1) was considered to be due to liver damage and increased AST and CK concentrations (Table 1) were thought to be linked to muscle tissue damage (Boyd 1983, Kerr 2002).

Transmission in TVT is through mucous membranes and it is easier in case of defective mucosal surface (Nak 2001). Such transmissions in oral, ocular and nasal mucosa are considered as extragenital TVT case (Parent et al 1983, Coskan et al 2011, Pigatto et al 2011). There is limited data available about the incidence of extragenital TVT cases since dogs with primary TVT are not necropsied. Most of the materials in the cases are through biopsy thus the rates of the metastasis to internal organs are not known (Gulbahar and Haziroglu 1995). The reported rate of metastasis in TVT cases is suggested to be higher because TVT cases in mucous membranes are not considered as metastatic and detailed ultrasonographical, radiographical examination and necropsy are not performed in most of the cases.

Metastasis rate in TVT cases are reported to be between 5-7% (Das and Das 2000, Purohit 2009). Metastasis occurrences in TVT cases are reported in tissues such as brain, adenohypophysis, udder, abdomen, inguinal subcutis, bone, eye and inguinal lymph node, spleen, uterus and ovarium (Adams and Slaughter 1970, Manning and Martin 1970, Oruc et al 2001, Rodrigues et al 2001, Nak et al 2004, Abuom and Mande 2006, Prihunkij et al 2006, Bastan et al 2008, Ozyurtlu et al 2008). Diffuse metastasis of TVT was reported in two male dogs and a bitch by some researchers (Gulbahar and Haziroglu 1995, Salt et al 2005, Park et al 2006). Although metastasis is in one or two organs in metastatic TVT cases, diffuse metastasis of TVT is

rarely observed. There was diffuse tumor metastasis in many organs such as skin, subcutis, udders, lymph nodes, last costa, abdomen, lung, liver and spleen in the presented case. In some cases, although there was metastasis in lung, it could not be diagnosed by radiographic examination (Salt et al 2005). Similarly, there was no sign of metastasis in radiographic examination of lung but it was discovered during macroscopy and pathological evaluations after necropsy. The metastatic mass was located in median lobe of the lung thus it was suggested that radiographic visualization may be compromised due to this localization.

It was reported that metastasis cases in TVT is rare, also metastasis to skin and lymph nodes are rare and metastasis to internal organs are not common too, however, it may metastasis to internal organs haematogenously and lymphogenously in case of immunosuppression (Rodrigues et al 2001, Park et al 2006). Following histopathological examinations, it was concluded that metastatic masses in internal organs was originated from vaginal TVT in this case (Figure 5b, 6b, 7b). Particularly, it was thought that TVT originated metastases in lung, liver and spleen was through haematogenous and lymphogenous pathway.

Although TVT is generally accepted as a benign tumor, sometimes it can be highly malign. The immune system has the most efficient role in that. Some immunological mechanisms limit spreading of the tumor while tumor specific antibodies cause its regression in animals with strong immune system. Tumor is usually malign in immunosuppressed animals and new metastases may cause (Adams and Slaughter 1970, Oruc et al 2001, Nak et al 2004). Immunosuppression may happen due to many factors such as pregnancy, lactation, viral, bacterial and parasitic chronic infections, insufficient feeding, drugs, toxins and stress (Dodds 2002). In the case presented, it was suggested that diffuse metastasis may have been occurred due to immunosuppression caused by postpartum period and lactation.

Eventually, it was observed that transmissible venereal tumor may





cause diffuse metastasis although reported rate is low. Thus, in dogs with TVT, a careful systemic examination and inquiring the presence of metastasis is suggested.

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