VETERİNER HEKİMLER DERNEĞİ DERGİSİ
JOURNAL OF THE TURKISH VETERINARY MEDICAL SOCIETY
ISSN: 0377-6395
e-ISSN: 2651-4214
Dergi ana sayfası /*Journal homepage:* http://dergipark.org.tr/vetheder
OPEN ACCESS

10.33188/vetheder.1329707

Olgu Sunumu / Case Report

A rare case of perivulvar hemangiosarcoma in a bitch

Zeynep GÜNAY UÇMAK [1,a*], Gülay YÜZBAŞIOĞLU ÖZTÜRK [2,b], İsmail KIRŞAN [1,c], Aslıhan BAYKAL [1,d], Ahmet GÜLÇUBUK [2,e], Egemen MAHZUNLAR [3,f]

[1] Department of Obstetrics and Gynaecology, Faculty of Veterinary Medicine, Istanbul University- Cerrahpaşa, Istanbul, Türkiye
[2] Department of Pathology, Faculty of Veterinary Medicine, Istanbul University- Cerrahpaşa, Istanbul, Türkiye
[3] Institute of Graduate Studies, Istanbul University- Cerrahpaşa, Istanbul, Türkiye
0000-0003-2530-1291[a]; 0000-0002-1761-0409 [b]; 0000-0003-0780-0118 [c]; 0000-0002-2107-1874 [d]; 0000-0002-9722-8831[e] ; 0000-0002-6815-6082 [f]

MAKALE BİLGİSİ / ARTICLE INFORMATION:

Geliş / Received:
19 Temmuz 23
19 July 23

Revizyon/Revised:
5 Eylül 23
5 September 23

Kabul / Accepted:
20 Eylül 23
20 September 23

Anahtar Sözcükler:
Dişi Köpek
Hemanjiosarkom
Immunohistokimya
Perivulvar

Keywords:
Bitch
Hemangiosarcoma
Immunohistochemistry
Perivulvar

ABSTRACT

An 11-year old, Rottweiler bitch was presented to the clinic with the complaint of a huge mass protruding from the left side of the vulvar labium. The bitch had been ovariohysterectomized due to the pyometra 2 years ago. The perivulvar mass was surgically removed by using an electrocautery device under general anesthesia. Macroscopically, the pedunculated mass was 20 cm x 25 cm in diameter, capsulated and slightly firm. Histopathological examination revealed that the mass was a hemangiosarcoma originating from the mucosa. Marked anisocytosis and anisokaryosis were noted in microscopic examination. Immunohistochemically, neoplastic cells showed positive staining for von-Willebrand factor-related antigen. On postoperative 3rd and 12th month follow-up protocols, the female dog was in good health condition and no metastases were detected in any organ. In this report, clinical follow-up, histological and immunohistological examination of a rare perivulvar hemangiosarcoma case in a female dog was presented.

Dişi bir köpekte nadir bir perivulvar hemanjiosarkom olgusu

ÖZET

Onbir yaşında, Rottweiler ırkı, dişi bir köpek vulvar labiumun sol yanından çıkıntı yapan kitle şikayeti ile kliniğimize getirildi. Köpeğe 2 yıl önce pyometra nedeniyle ovariohisterektomi uygulanmıştı. Genel anestezi altında elektrokoter cihazı kullanılarak perivulvar kitle cerrahi olarak çıkarıldı. Makroskopik olarak 20 cm x 25 cm çapında, kapsüllü ve hafif sert saplı kitle görüldü. Histopatolojik incelemede, kitlenin mukozadan köken alan bir hemanjiyosarkom olduğu saptandı. Mikroskobik incelemede belirgin anizositoz ve anizokaryoz kaydedildi. İmmünohistokimyasal olarak neoplastik hücreler, von-Willebrand faktörü ile ilişkili antijen için pozitif boyanma gösterdi. Operasyon sonrası 3. ve 12. ay takip protokollerinde köpeğin sağlık durumu iyiydi ve herhangi bir organa metastaz göstermedi. Bu olgu sunumunda, dişi bir köpekte nadir görülen bir perivulvar hemanjiyosarkom olgusunun klinik takibi, histolojik ve immünohistolojik bulguları sunulmuştur.

How to cite this article: Uçmak Günay Z, Öztürk Yüzbaşıoğlu G, Kırşan İsmail, Baykal A, Gülçubuk A, Mahzunlar E. A rare case of perivulvar hemangiosarcoma in a bitch. Vet Hekim Der Derg 95 (1): 60-65, 2024. DOI: 10.33188/vetheder.1329707

* *Sorumlu Yazar e-posta adresi / Corresponding Author e-mail address*: *zeynep.gunayucmak@iuc.edu.tr*

1. Introduction

Hemangiosarcomas (HSA) are malignant tumors of endothelial cells which are usually spindle-shaped in appearance (1). The mean age of diagnosis ranges from 9 to 12 years in dogs (2). Although no sex and breed predisposition are specified, German Shepherd, Boxer, Great Dane, Golden Retriever, English Setter and Pointer breeds have increased incidence (3). Though the primary involvement site is the spleen, HSA can affect the liver, heart, lungs, kidneys, skin, oral cavity, muscle, and peritoneum (3-5). Although visceral HSAs are very aggressive tumors with high mortality rates, dermal HSAs have lower metastatic potential and less aggressive biological behaviour (2, 4, 6). Compared to visceral hemangiosarcomas, cutaneous hemangiosarcomas are less aggressive and show a low metastasis rate. It has been reported that chronic solar irradiation can be the cause of dermal hemangiosarcoma (7). It was aimed to report clinical follow-up, histological and immunohistological examination of a rare perivulvar hemangiosarcoma case in a bitch.

2. Case Story

An 11-year-old, Rottweiler bitch was presented to the clinic with the history of a large tumor mass protruding from the left side of the vulvar labium. The owner noticed the perivulvar mass one year ago when it was approximately three cm in diameter vertically. However, any treatment had not been applied at this time. The tumoral mass was approximately 25 cm in diameter (Figure 1A.), capsulated and had a slightly firm structure. The bitch had been ovariohysterectomized due to the pyometra 2 years ago.

Figure 1: (a) A huge mass on the left perivulvar area, **(b)** Image of the operation area after the mass was surgically extirpated.

Şekil 1: (a) *Sol perivulvar bölgede büyük bir kitle,* ***(b)*** *Kitle cerrahi olarak çıkarıldıktan sonra operasyon bölgesinin görüntüsü.*

Clinical examination and treatment

Complete blood count (CBC) and biochemical parameters (glucose, creatinine, blood urea nitrogen, blood urea nitrogen/creatinine (BUN/CREA), total protein, globulin, albumin, albumine/globuline (ALB/GLOB), alanine aminotransferase, alkaline phosphatase, calcium and inorganic phosphorus) were within normal limits. There was no evidence of vaginal disorders such as hyperplasia, prolapses or tumor in the vaginal examination. Three-view thoracic radiography and abdominal ultrasonography were applied to determine the presence of any metastasis. Any metastatic foci were not visualized on abdominal organs and thorax. General anesthesia was induced by 1% propofol (4 $mg.kg^{-1}$, iv) (Lipuro®, Braun, England) and maintained with 3% isoflurane (Forane likid®, Abbott Laboratories, England) and 2% oxygen combination. The perivulvar mass was surgically removed by using an electrocautery device. The skin was sutured with an absorbable material (Monocryl No:2/0, Medeks, Turkey) by subcutaneous simple continued route (Figure 1B.). The suture line healed within ten days. For postoperative care; enrofloxacin 5% (5 $mg.kg^{-1}$, sc, s.i.d.) (Bayrtil-K® 5%, Bayer, Türkiye), vitamin B12 (40 $mcg.kg^{-1}$, im, s.i.d.) (Dodex®, Deva, Türkiye), sucralfate (1 g, per

dog, oral, s.i.d.) (Antepsin®, Bilim İlaç, Türkiye) and meloxicam (0.2 mg.kg^{-1}, sc, s.i.d.) (Maxicam®, Sanovel, Türkiye) were prescribed for a week.

Histopathological examination

Surgically removed tissues were submitted to the pathology department of our faculty for histopathological examination. Tissue samples were fixed in 10% neutral buffered formalin. After being routinely processed they were embedded in paraffin. Sections cut at 4 μm in thickness were stained with Hematoxylin&Eosin (H&E) to be evaluated with light microscopy. Tissue sections were immunohistochemically stained with anti-von Willebrand (vWF) factor antibody (1:1000; rabbit polyclonal, Ab6994; Abcam) using streptavidin–biotin–peroxidase method described before (7). Macroscopically, the pedunculated mass was 20 cm x 25 cm in diameter, capsulated and slightly firm. The cut surface was hemorrhagic and contained black colored areas.

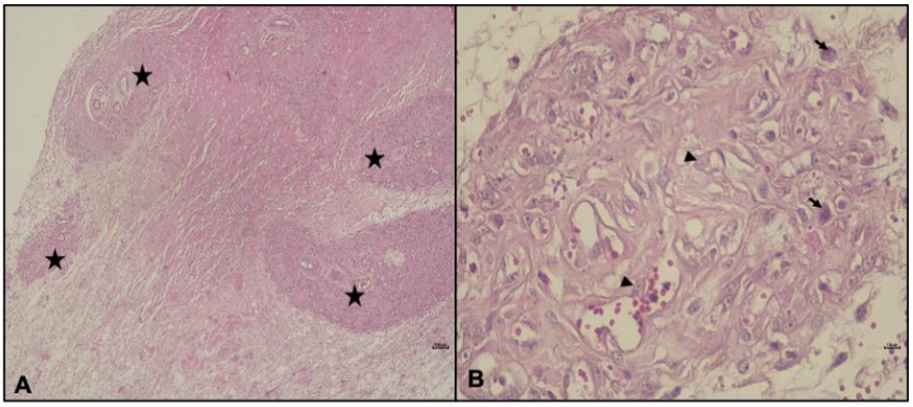

Figure 2. (a) The neoplasm is composed of islets of neoplastic cells (stars) scattered in loose collagen. H&E, Bar = 1000 μm, **(b)** Pleomorphic neoplastic cells that formed the irregular vascular spaces and irregular shaped vascular channels filled with red blood cells (RBCs) in their lumens (arrowhead). Marked anisocytosis, anisokaryosis and mitotic figures (arrow) are seen. H&E, Bar=10 μm.

Şekil 2. (a) *Neoplazm, gevşek kollajen içinde dağılmış neoplastik hücre adacıklarından (yıldızlar) oluşur. H&E, Bar = 1000 μm,* ***(b)*** *Düzensiz vasküler boşlukları ve lümenlerinde kırmızı kan hücreleriyle dolu düzensiz şekilli vasküler kanalları oluşturan pleomorfik neoplastik hücreler (ok başı). Belirgin anizositoz, anizokaryoz ve mitotik figürler (ok) görülüyor. H&E, Bar=10 μm.*

Histopathological analysis revealed that the extirpated mass was a hemangiosarcoma, originating from the mucosa of the perivulvar area. Histologically, the tumor consisted of haphazardly scattered islets of different sizes in loose collagen (Figure 2A.). The neoplastic cells that formed the irregular vascular spaces were varying from spindle to polygonal in shape with small to moderate amounts of eosinophilic cytoplasm and indistinct cytoplasmic borders. The nuclei of individual cells were hyperchromatic, round to oval, containing 2-3 prominent nucleoli. Marked anisocytosis and anisokaryosis were noted (Figure 2B.). Mitosis was few with 3 per 10 high-power field. Immunohistochemically, neoplastic cells showed positive staining for von-Willebrand factor-related antigen (Figure 3A. and Figure 3B.).

Abdominal ultrasonography, thoracic radiography, hemogram and some biochemical parameters were performed three months after the operation to check for metastases and no suspicious mass was observed. Similarly, the female dog was found to be in good health at the follow-up one year later.

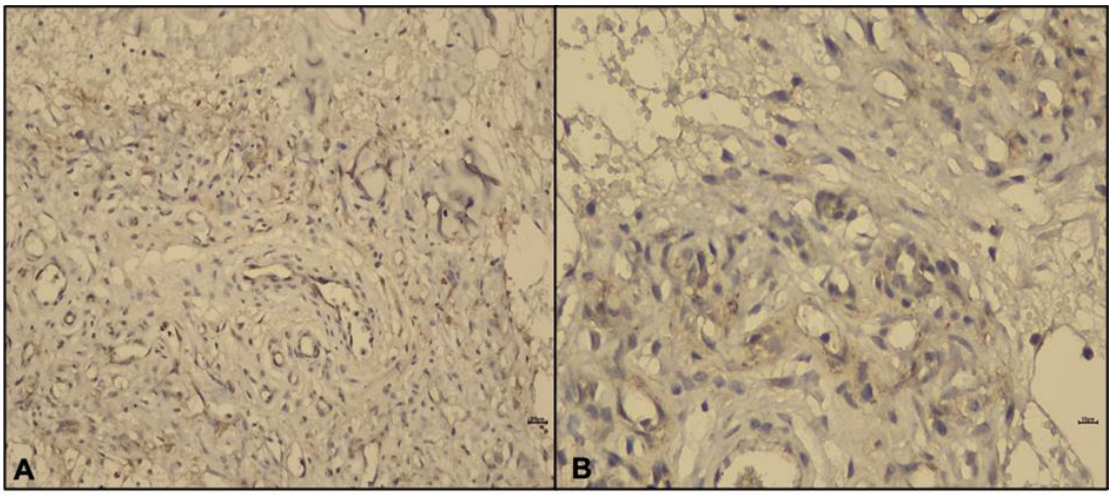

Figure 3: Immunohistochemical staining of the neoplastic cells for von Willebrand Factor (vWF). Positive reaction were observed in tumor cells as intracytoplasmic brown granules. The sections were counterstained with Mayer hematoxylin. **(a)** Bar = 20 µm and **(b)** Bar= 10 µm

Şekil 3: *Von Willebrand Faktörü (vWF) için neoplastik hücrelerin immünohistokimyasal boyanması. Tümör hücrelerinde intrasitoplazmik kahverengi granüller halinde pozitif reaksiyon gözlendi. Kesitler, Mayer hematoksilin ile karşıt boyamaya tabi tutuldu.* ***(a)*** *Bar = 20 µm ve* ***(b)*** *Bar = 10 µm*

3. Discussion and Conclusion

The incidence of HSA is high in dogs than any other animal species (3). The occurrence of HSAs has usually been reported in dogs older than 8 years of age (2,3). In consistent with the previous reports, this dog with perivulvar hemangiosarcoma was 11 years old. Although no breed predisposition was specified in the literature (3), Rottweiler was not one of the breeds that had increased incidence. Studies showed that neutering increase HSA development especially in the spleen and heart. Hormonal association with canine HSA has been reported with regard to spaying, and female dogs spayed at a later age have a higher percentage of HSA development compared to female dogs spayed at an early age (8,9). Spayed female dogs have 5 times more risk of HSA than intact female dogs (10). Torres de la Riva et al. (8) suggested, cells that become sensitive to estrogen as a result of multiple cycles may undergo neoplastic transformation with the disappearance of the protective effect of estrogen after sterilization. In this case, HSA developed 2 years after the female dog has been neutered at 9 years old.

HSAs are malignant tumors of vascular endothelial cells (1). In the current case, the histomorphological findings such as marked anisocytosis, anisonucleosis, and irregular vascular canals surrounded by polymorphic neoplastic cells confirmed the tumor as HSA. Azizi et al. (11) considered the presence of blood vessels of different sizes lined by polymorphic endothelial cells as evidence of malignancy. Von-Willebrand factor antibody has been used to identify vascular neoplasms in dogs (12). Immunohistochemical examination of neoplastic cells showed a positive reaction to the von-Willebrand factor.

Although anemia and neutrophilic leukocytosis were the most common hematological abnormalities of HSA (13), CBC and biochemical parameters were determined within reference ranges in this case. However, CBC parameters became close to the upper limit of the reference range one month after the surgical removal of the perivulvar mass. An increase in hematological parameters may have occurred as a result of the presence of a large amount of bleeding focus in HSA tumors and the elimination of blood accumulation with tumor excision as Brown (4) reported. In dogs, the most common primary sites for HSA are the spleen, liver and right auricle of the heart, although primary dermal HSAs have also reported (3-5). Primary HSAs of the vagina are quite rare in both domestic animals and humans. There are case reports of vulvar HSA in a dog (14), cow (15) and mare (16) in the literature. In this report, a rare case of HSA in perivulvar mucosa of a female dog is presented. The main mechanisms of metastasis of HSA are via the

hematogenous route and the common sites of metastasis are the lung, liver and omentum (17). Cutaneous HSA tends to have a lower metastatic rate, and they are generally associated with longer survival times (2). Also, lung metastasis and atrial metastasis were not observed in a female dog with vulva-vaginal hemangiosarcoma (14). In this case, no metastasis was found in the clinical examinations performed during one year after the surgical intervention. There were several reports on the treatment of HSA with chemotherapy, antiangiogenic drugs, surgery or their combinations (18,19). Treatment with surgery and chemotherapy (doxorubicin) combination was provided longer survival time compared to the dogs treated with surgery alone (274 days versus 66 days) (19). Sorenmo et al. (18) reported that median survival times in dogs with HSA treated with surgery alone were 3 weeks to 2 months whereas the median survival times of the dogs treated with surgery and chemotherapy combination were 3 to 6 months. In this case, only surgery was performed as a treatment of HSA and unlike with Sorenmo et al. (18), the dog is still alive although one year has passed since treated surgically. It was concluded that HSA cases could be treated by surgery alone but it should be followed-up regularly during the post-operative life time.

Conflict of Interests

There is no personal or financial conflict of interest between the author(s) of the article within the scope of the study.

Funding

During this study, any pharmaceutical company that has a direct connection with the subject of the research, a company that provides and/or produces medical instruments, equipment and materials, or any commercial company, during the evaluation process of the study, will receive financial and/or any moral support that may adversely affect the decision to be made regarding the study.

Authors' Contributions

Motivation / Concept: Zeynep Günay Uçmak, Gülay Yüzbaşıoğlu Öztürk
Design: İsmail Kırşan, Ahmet Gülçubuk
Control/Supervision: İsmail Kırşan, Ahmet Gülçubuk
Data Collection and / or Processing: Aslıhan Baykal, Egemen Mahzunlar
Analysis and / or Interpretation: Zeynep Günay Uçmak, Gülay Yüzbaşıoğlu Öztürk
Literature Review: Zeynep Günay Uçmak, Gülay Yüzbaşıoğlu Öztürk
Writing the Article: Zeynep Günay Uçmak
Critical Review: Gülay Yüzbaşıoğlu Öztürk, İsmail Kırşan

Ethical Approval

An ethical statement was received from the authors that the data, information and documents presented in this article were obtained within the framework of academic and ethical rules, and that all information, documents, evaluations and results were presented in accordance with scientific ethics and morals.

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