



## CASE REPORT

### A case of plasmacytoma with widespread metastasis in a dog

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### Bir köpekte yaygın metastazlı plazmasitom olgusu

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#### Öz

Bu çalışmada, dokuz yaşında Rottweiler ırkı erkek bir köpekte rastlanan yaygın metastazlı plazmasitom olgusu histopatolojik ve immunohistokimyasal yöntemlerle tanımlanmıştır. Makroskopik muayenede akciğer, karaciğer, mediastinal ve mezenteriyal lenf düğümleri, dalak, kalp, pankreas, bağırsak ve böbreklerde 0,5-3 cm arasında değişen büyüklüklerde multifokal yerleşimli beyaz veya pembe-kırmızı renkli kitleler tespit edildi. Mikroskopik muayenede akciğer, karaciğer, dalak, pankreas, mediastinal ve mezenteriyal lenf düğümleri, bağırsak ve böbreklerde çoğunluğu atipik plazma hücrelerinden oluşan tümör odakları gözlemlendi. Akciğerdeki tümör odaklarında tümör tipi dev hücrelerine, akciğer dahil incelenen diğer organlardaki tümör odaklarında mitotik figürlere ve kapillar damarların içinde bol miktarda tümör hücrelerine rastlandı. Akciğer, karaciğer, dalak, pankreas, mediastinal ve mezenteriyal lenf düğümleri, bağırsak ve böbrek kesitlerinin Methyl Green Pyronin boyamalarında plazma hücrelerinin sitoplazmasının pembe renkte boyandığı görüldü. Karaciğer ve dalak kesitlerine yapılan Congo Red boyamasında kiremit kırmızısı renkte boyanan amiloid birikimlerinin olduğu gözlemlendi. Ayrıca akciğer, karaciğer, dalak, pankreas, mediastinal ve mezenteriyal lenf düğümleri, bağırsak ve böbrek kesitlerinin Proliferating Cell Nuclear Antigen (PCNA) antikoruna ile immunohistokimyasal boyamasında tümör hücrelerinde şiddetli immunoreaktivite belirlendi. Sonuç olarak teşhis edilen plazmasitom olgusunun akciğer, karaciğer, dalak, pankreas, mediastinal ve mezenteriyal lenf düğümleri, bağırsak ve böbreklerde nadir bildirilen yaygın metastazların bulunması nedeniyle veteriner hekimlerin dikkatinin çekilerek literatüre katkı sağlanması amacıyla vakanın yayınlanması uygun görülmüştür.

**Anahtar kelimeler:** Histopatoloji, İmmunohistokimya, Köpek, Metastaz, Plazmasitom

#### Abstract

In this study, a case of plasmacytoma with widespread metastasis in a nine-year-old male Rottweiler dog was described by histopathological and immunohistochemical methods. Macroscopic examination revealed multifocal white or pink-red colored masses ranging in size from 0,5 to 3 cm in the lung, liver, mediastinal and mesenteric lymph nodes, spleen, heart, pancreas, intestine and kidneys. In microscopic examination, tumor foci consisting mostly of atypical plasma cells were observed in the lung, liver, spleen, pancreas, mediastinal and mesenteric lymph nodes, intestine, and kidneys. Tumor-type giant cells were observed in tumor foci in the lung, mitotic figures in tumor foci in other organs, including the lung, and abundant tumor cells in capillary vessels. In Methyl Green Pyronin staining of lung, liver, spleen, pancreas, mediastinal and mesenteric lymph nodes, intestine and kidney sections, the cytoplasm of plasma cells was observed to be stained pink. Congo Red staining applied to liver and spleen sections showed amyloid deposits stained in brick red color. In addition, in the immunohistochemical staining of lung, liver, spleen, pancreas, mediastinal and mesenteric lymph nodes, intestine and kidney sections with Proliferating Cell Nuclear Antigen (PCNA) antibody, severe immunoreactivity was detected in tumor cells. As a result, due to the presence of rarely reported widespread metastases in the lung, liver, spleen, pancreas, mediastinal and mesenteric lymph nodes, intestine and kidneys of the diagnosed plasmacytoma case, it was deemed appropriate to publish the case in order to contribute to the literature by attracting the attention of veterinarians.

**Keywords:** Dog, Histopathology, Immunohistochemistry, Metastasis, Plasmacytoma.

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## Introduction

Plasma cell tumors are characterized by proliferation of neoplastic monoclonal plasma cells (Tong et al 1980, Dimopoulos and Hamilos 2002). Multiple myeloma is a clinically important form of plasma cell tumor in dogs and is often associated with dysregulated immunoglobulin secretion from neoplastic plasma cells in the medullary space of bone (Morris and Dobson 2001, Adelman et al 2014). Plasma cell tumors are tumors that are located in soft tissues and organs outside the bone marrow, have spread to regional lymph nodes or can metastasize to distant organs (Adelman et al 2014). In the study of Kupanoff et al (2006), a total of 56,175 biopsy samples taken from dogs had been examined by the Pathology Laboratory of the University of Pennsylvania School of Veterinary Medicine between 1998-2001 and 55% of the total biopsy samples were tumoral cases; 751 of these cases had been determined to be plasmacytoma cases. Kupanoff et al (2006) evaluated 751 plasmacytoma cases in dogs and found that 86% were located in the skin, 9% in the mucous membranes, and 4% in the rectum and colon. The same researchers reported that cases in organs such as stomach, spleen, genital organs, eye, uterus and liver accounted for 1% of total plasmacytoma cases (Kupanoff et al 2006).

Plasmacytomas account for approximately 2,5% of all tumors in dogs. The majority of plasma cell tumors occur in older dogs (Clark et al 1992). In plasmacytoma cases, macroscopically, numerous round tumoral foci of and different sizes are encountered. In addition, the cross-sectional surface of the tumor is white or pink-red. Although the macroscopic appearance of plasmacytoma is similar to histiocytoma, its histological differences are evident microscopically. In plasmacytoma, tumor cells are similar to normal plasma cells, but these cells are seen in larger sizes. Despite the nuclear pleomorphism of neoplastic plasma cells, the cells usually have little or moderately eosinophilic cytoplasm. Anisocytosis and anisonucleosis are moderate, and mitotic activity is usually low. Sometimes abnormally shaped giant cells may also be found. In plasmacytoma cases, amyloid deposits are typically encountered between cells, in vessels, or around the tumor. The amyloid that has accumulated is immunoglobulin-mediated (primary) amyloid (Baer et al 1989, Hendrick 2016, Erer and Kiran 2019).

In this case report, it is aimed to describe a case of widespread metastasized plasmacytoma in a dog and to pay attention to extracutaneous plasmacytoma by clinician veterinarians.

## Case Presentation

An opaque lesion in the left cranial lobe of the lung was detected in the thorax radiograph of a nine-year-old Rottweiler male dog who submitted to the clinic with

complaints of loss of appetite and respiratory distress, and fluid accumulation in the thorax was observed. The dog that died while the fluid was drained with thoracentesis was brought to the Pathology Department for necropsy.

In systemic necropsy; a white-pink mass of 1-2 cm in size was detected in the left cranial lobe of the lung (Figure 1-A). In addition, hydrothorax was observed. Multifocal white masses 0,5-2 cm in size were seen in the spleen. In the extremitas ventralis of the spleen, a swelling with a dark red color and hard-consistent was observed on the cross-sectional surface covering one-fifth of the spleen (Figure 1-B). Enlargement of the mediastinal and mesenteric lymph nodes and white masses 1-2 cm in size were seen (Figure 1-C). Multifocal masses 0.5-1 cm in size were identified in the kidneys. In addition, areas of necrosis were seen in the kidneys extending to the pelvis (Figure 1-D). The liver was found to be quite enlarged, with blunt edges. The pancreas was observed to be quite enlarged, and masses of 1-3 cm in size were detected in the pancreas. Fluid accumulation in the pericardial cavity and petechial hemorrhage areas in the epicardial layer of the heart were observed. In addition, 0,5 cm in size white masses were seen in the heart's interventricular muscles. Thickening of the intestinal was observed and small white masses were detected in the intestinal serosa. No tumoral findings were found in the bone marrow.

For histopathological and immunohistochemical examinations, samples taken from lung, liver, spleen, heart, pancreas, intestine, mediastinal and mesenteric lymph nodes and kidneys were fixed in 10% buffered formalin solution. After routine tissue processing procedure, sections of 5 µm thickness were taken from the paraffin-blocked tissues with a microtome and stained with Hematoxylin-Eosin (HE), Methyl Green Pyronin (MGP), Congo Red (CR) and Periodic acid-Schiff (PAS) (Luna 1968). In addition, selected tissue sections were immunohistochemically stained using monoclonal anti-Proliferating Cell Nuclear Antigen (PCNA) primary antibody (1:200, Dako, M0879) according to the previously reported method (Akçakavak et al 2023). The slides were examined under a light microscope and photographed.

In histopathological; examination of the mass determined in the lung revealed many atypical plasma cells with anisocytosis and anisonucleosis, tumor-type giant cells with many nuclei, high mitotic activity and abundant tumor cells in the capillary vessels (Figure 2-A, B). Thickening of the interalveolar septum in the lung, and mononuclear cell infiltration around the bronchi and bronchioles were determined. An infarct area was observed in the kidney, as well as atypical tumor cells and numerous mitotic figures were observed in the intertubular areas next to the infarct area. A thickening of the basement membrane was observed

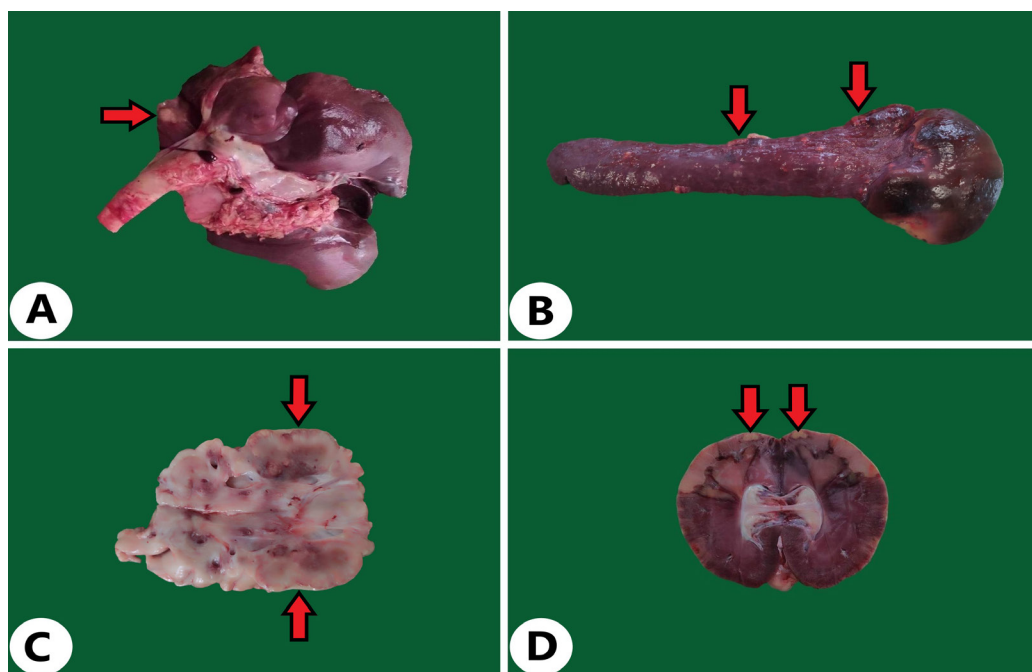


Figure 1. Macroscopic findings. A: 2 cm in size white-pink mass in the left cranial lobe of the lung (red arrow), B: Multifocal white-pink masses of 0.5-2 cm in the spleen (red arrows), C: Cross-sectional view of 1-2 cm white masses (red arrows) and enlargement in the mesenteric lymph node, D: Cross-sectional view of 1 cm mass in the kidney (red arrows).

in the kidney (Figure 2-C, D). Tumor cells were detected to be localized in the sinusoids of the liver (Figure 2-E). In the liver, dissociation of the remark cords, and mononuclear cell infiltrations were observed in the portal area. Tumor cells were observed in the sinusoids of the spleen. In addition, thickening of the spleen capsule and necrotic areas in the subcapsular region were determined. Loss of striation in cardiac muscle cells and cell infiltrations, including diffuse tumor cells, were observed between muscle bundles. Cell clusters with an abundance of tumor cells were determined in the capillary vessels between the muscle bundles. Cell infiltrations including all layers of the intestine were found, especially in the epithelial layer of the intestine. Numerous mitotic activities were detected with pleomorphic tumor cells in cell infiltrations in the epithelial layer of the intestine. A large number of tumor cells were found that diffuse to the pancreatic parenchyma. It was observed that there were many mitotic activities in these areas of the pancreas, as well as pleomorphic tumor cells with nuclei of different sizes and different staining properties. Diffuse tumor cells were found in mediastinal and mesenteric lymph nodes. In addition, high mitotic activity and tumor cells in capillary vessels were detected in lymph nodes.

In Methyl Green Pyronin (MGP) staining performed to show plasma cells in lung (Figure 2-F), liver, spleen, heart, pancreas, intestine, mediastinal and mesenteric lymph nodes and kidney sections, the cytoplasm of plasma cells was stained pink. In Congo Red staining performed on liver and spleen sections to determine amyloid deposits, it was observed that there were amyloid deposits stained in brick

red colour in the sinusoids (Figure 2-G). Periodic acid-Schiff (PAS) staining of kidney sections revealed thickened basement membrane (Figure 2-H).

Severe immunoreactivity was detected in tumor cells in immunohistochemical staining of kidney (Figure 2-I), lung, liver, spleen, pancreas, intestine, mediastinal and mesenteric lymph nodes and heart sections with PCNA antibody.

Plasmacytomas are commonly seen in 8-10 year old dogs (Baer et al 1989, Clark et al 1992, Cangul et al 2002). In this case, seen in a 9-year-old dog, similar to the literature data. According to literatur, 4% of canine plasmacytomas are observed in the rectum and colon, 9% in the mucous membranes and 86% in the skin. Additionally, the remaining 1% of canine plasmacytomas have been reported to occur in other organs, including the stomach, spleen, reproductive organs, eyes, uterus and liver (Kupanoff et al 2006). Although it was reported that cutaneous plasmacytoma cases were the most common in terms of localization, multiple organ plasmacytoma including lung, liver, spleen, heart, pancreas, intestine, mediastinal and mesenteric lymph nodes and kidneys was determined in this case without skin lesion.

Plasmacytomas are tumors that are focally located in organs and can metastasize to distant tissues and organs (Adelman et al 2014). In this case, the presence of tumor cells in the vessels and the presence of tumoral lesions in many organs indicate that the tumor has metastasized. PCNA activity is one of the nuclear markers that show tumor grade, recurrence

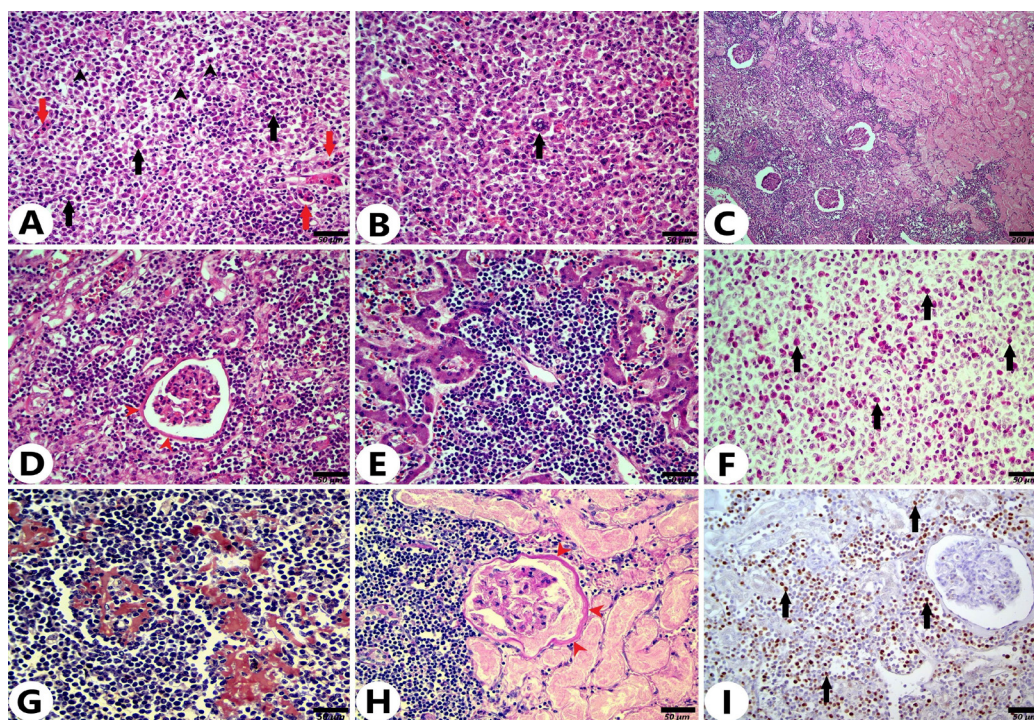


Figure 2. Histopathological and immunohistochemical findings. A: Many atypical plasma cells (black arrows) with anisocytosis and anisonucleosis, mitotic figures (black arrowheads) and abundant tumor cells in the capillary vessels (red arrows), HE, x40, B: Tumor type giant cell (black arrow) and many atypical plasma cells in the lung, HE, x40, C: General view of the tumoral area next to the infarct area in the kidney, HE, x10, D: Thickening of the basement membrane in the kidney (red arrowheads) and tumor cells in the intertubular areas, HE, x40, E: Tumor cells in liver sinusoids, HE, x40, F: Pink staining of the cytoplasm of plasma cells in the lung (black arrows), MGP, x40, G: Amyloid deposition in the spleen, Congo Red, x40, H: Basal membrane thickening in kidney (red arrowheads), PAS, x40, I: Severe immunoreactivity in tumor cells against PCNA antibody in the kidney (black arrows), IHC, x40.

rate, and tumor aggressiveness (Kayaselcuk et al 2002). In our case, the high PCNA reactivity observed in tumor cells supports the aggressiveness and malignancy of the tumor.

Histopathologically, it is reported that tumor cells have eosinophilic cytoplasm and anisocytosis, anisonucleosis and mitotic figures are seen in plasmacytomas. It has also been reported that many cells have numerous nuclei (Adelman et al 2014, Hendrick 2016, Erer and Kiran 2019). In our case, similar to the literature data, tumor cells were encountered and high mitotic activity was observed. In addition, tumor-type giant cells with multiple nuclei were also found.

In plasmacytoma cases, there are usually amyloid deposits between cells, around the vessels or tumor (Hendrick 2016, Erer and Kiran 2019, Ates et al 2019, Ates et al 2019a, Ortatatl et al 2021). In this case, amyloid deposits were observed in the spleen and liver together with multiple organ plasmacytoma.

Membranous glomerulonephritis is an immune complex nephropathy characterized by glomerular basement membrane thickening as a result of deposition of subepithelial immunoglobulin and its complement components. In membranous glomerulonephritis cases, glomerular basement membrane thickening is seen in kidney sections stained with Hematoxylin-Eosin or Periodic acid-Schiff (Beck Jr and Salant 2010, Hatipoglu and Erer 2017). In

our case, basement membrane thickening was observed as a result of staining the kidney with Hematoxylin-Eosin and Periodic acid-Schiff because of subepithelial accumulation of increased immunoglobulin due to plasmacytoma.

As a result, this case was diagnosed with plasmacytoma by pathological and immunohistochemical evaluations. Although plasmacytoma can occur in many organs and tissues, it is very important to draw the attention of clinician veterinarians to these cases, since its incidence is low in the lung, liver, spleen, heart, pancreas, intestine, mediastinal-mesenteric lymph nodes and kidneys.

#### Conflict of Interest

The authors did not report any conflict of interest or financial support.

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### Author Contributions

Motivation/Concept: MT, ZC, OD, AT, FMO; Design: OD; Control/Supervision: MT, ZC; Data Collection and/or Processing: OD, AT, FMO; Analysis and/or Interpretation: MT, ZC, OD; Literature Review: OD, AT, EG; Writing the Article: OD, AT, FMO; Critical Review: MT, ZC.

### Ethical Approval

Selcuk University Faculty of Veterinary Medicine Experimental Animal Production and Research Center Ethics Committee (SÜVDAMEK) decided that "There is no need for an Ethics Committee Decision" (Decision No: 2023/583162).

