



## Case Report

# Histopathological case study of canine hemangiosarcoma with multiple organ metastases

Belén Varela<sup>1</sup>, Camila Larrañaga<sup>1</sup>, Kanji Yamasaki<sup>1</sup>, José Manuel Verdes<sup>1\*</sup>

<sup>1</sup>Pathology Unit, Department of Pathobiology, Faculty of Veterinary, Universidad de la República (Udelar).  
Route 8 km.18 and Route 102, CP 13000, Montevideo, Uruguay.

\*Corresponding author: E-mail: [jmverdes@fvvet.edu.uy](mailto:jmverdes@fvvet.edu.uy)

Submitted July, 15<sup>th</sup> 2022, Accepted August, 30<sup>th</sup> 2022

---

### Abstract

We studied a 14-year-old male dog necropsied. Gross findings were hemorrhagic nodules in the spleen, liver, heart and abdominal and thoracic lymph nodes. Histologically, we homogeneously observed tumor cells often with prominent, bulging and mitotic nuclei that were pleomorphic and hyperchromatic, forming small blood vessels. Tumors in all organs were diagnosed as capillary hemangiosarcomas. No tumor cells were detected in the lungs. We presume that the primary tumor was present in the spleen, from where it metastasized multiple organs via lymphatic vessels.

**Key words:** dog, pathology, hemangiosarcoma, spleen.

---

### Introduction

Hemangiosarcomas are the most common primary malignant tumors occurring in the spleen of dogs (3, 6, 11, 13), and is capable of metastasizing various organs (14). Splenic hemangiosarcomas were reported usually metastasize the heart in than 25% of cases (2). It was also described that metastases of splenic hemangiosarcomas differ between small and large dogs, the later showing metastases in the abdominal and/or thoracic organs, muscles and subcutaneous flank (14). Canine hemangiosarcomas present in general high possibility of producing metastases, and primary hemangiosarcomas of organs other than the spleen are also known to metastasize as well (4, 8-10, 15, 16, 18). In this work, we present a diagnosis of capillary hemangiosarcoma in an old, crossbred dog, that affected the spleen, liver, heart and abdominal and thoracic lymph nodes. The main purpose of this study is to characterize the morphological changes produced by the hemangiosarcoma in the different organs.

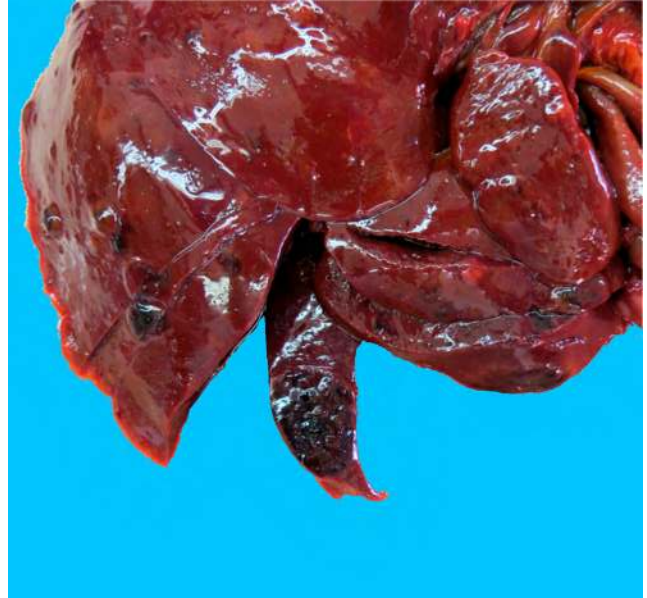
### Case Description

The studied specimen was a crossbred, 14 year old male dog of large size (ca. 30 kg). General signs prior to death were disorexia to anorexia, polydipsia, oliguria, and ascites. Ultrasonographic evaluation of the patient allowed to detect nodules in the liver and spleen. The dog received symptomatic treatment, but the condition did not improve and died. Abnormal tissues found at necropsy were fixed in 10% neutral buffered formalin solution, processed, sectioned at 4 µm, and stained with hematoxylin-eosin (HE). Histological examination was performed under light microscopy by 3 experienced veterinary pathologists.

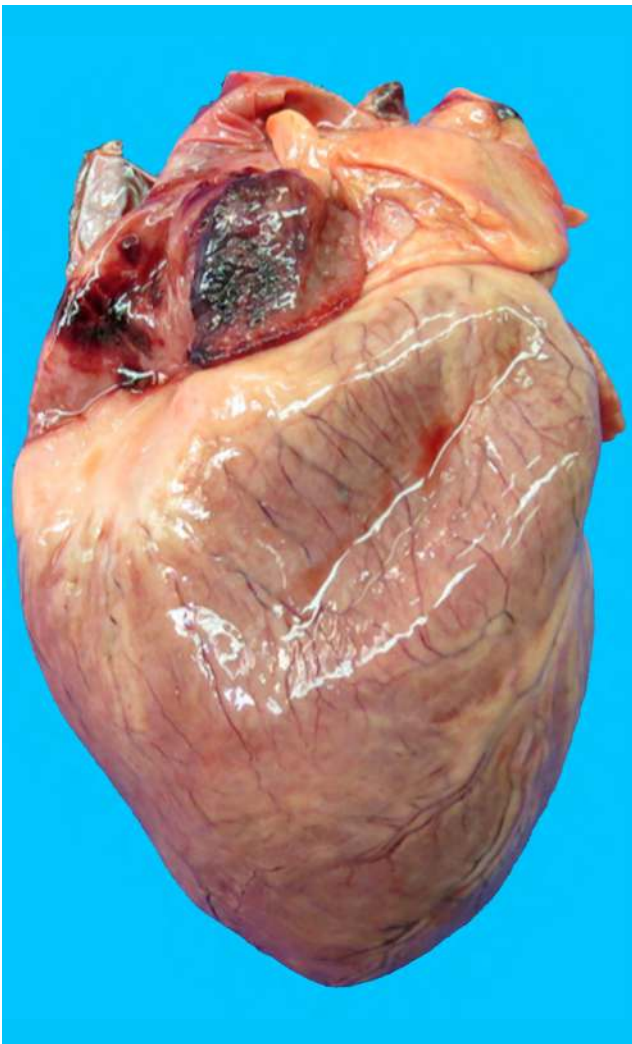
Grossly, mild bloody ascites and pericardial fluid were detected. Multiple nodules of various sizes were observed in the spleen, from less than 0.5 cm to approximately 10 cm in diameter (Fig. 1). Although a particular structure was not evident on the cut surface of these tumors, hemorrhage was a characteristic and constant finding. We found nodules of various sizes both in the liver and spleen



**Figure 1.** Spleen. Nodules of various sizes.

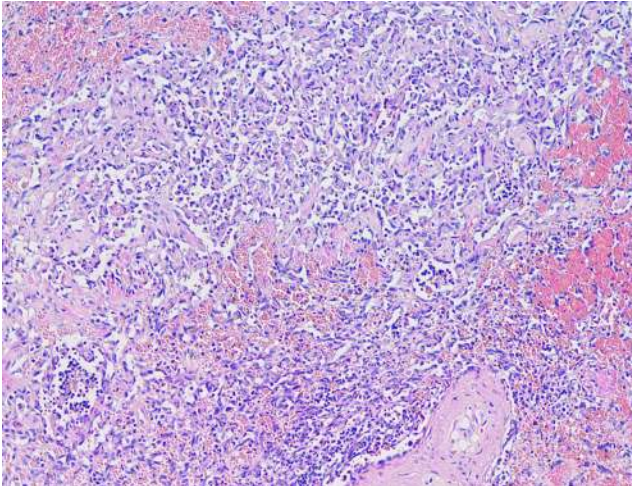


**Figure 2.** Liver. Nodules of various sizes.

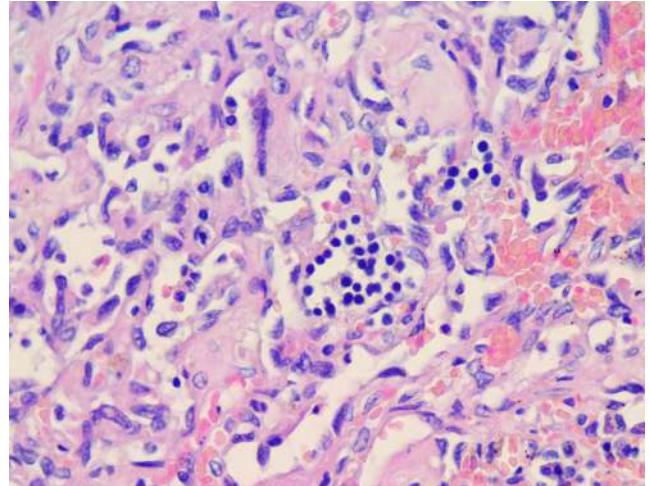


**Figure 3.** Heart. Nodular lesion in the right atrium.

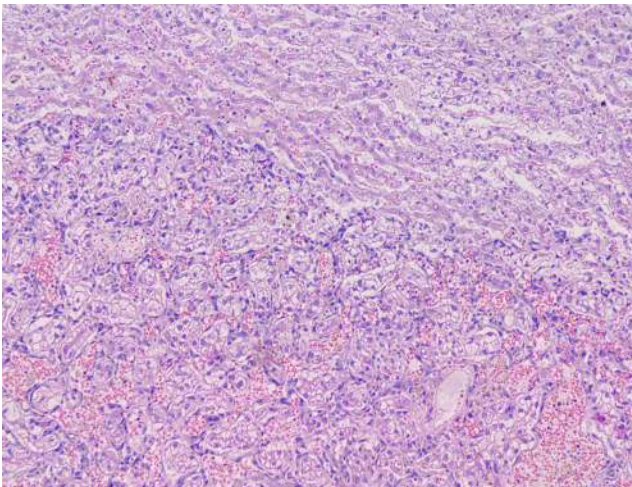
(Fig. 2). Hemorrhage was seen in the right atrium with a tumoral mass proliferation spreading to the surrounding muscular wall (Fig. 3). The thoracic and abdominal lymph nodes, especially the mediastinal and mesenteric ones, were swollen and hemorrhagic. Congestion and edema were observed in the lungs, but no gross nodules were detected. Histologically, tumor cells proliferating in the spleen, liver, heart and lymph nodes were identified. The morphology of tumor cells in each organ was basically the same, and often presented a prominent, bulging nuclei, that were pleomorphic and hyperchromatic, commonly with mitosis. The tumor cells formed small blood vessels, some of them associated to hemorrhagic lesions. In the spleen, the normal structure of the organ disappeared, and was completely replaced by tumor cells in main tumor growth areas (Figs. 4 and 5). Necrosis and hemorrhage were more evident as extensive proliferation of tumor cells was observed. In the liver, these cells became clumpy and pressed the surrounding tissue with degeneration and necrosis of hepatocytes; infiltration of tumor cells into the sinusoids was also evident (Figs. 6 and 7). In the heart, tumor cells similar to those in the spleen and liver were seen infiltrating myocardial fibers, causing atrophy and degeneration (Figs. 8 and 9). Formation of capillaries by tumor cells was observed in some areas. In all lymph nodes, the cells infiltrated the dilated sinus, which was accompanied by the formation of miriads of capillaries plus hemorrhage (Fig. 10). Tumor cells at these locations were predominantly round, oval, spindle-shaped with distinct atypical nuclei, and often bearing mitotic figures. The lungs showed congestion and edema, but with no neoplastic changes neither observed at gross pathology nor histology. In summary, the overall pattern of growth of the hemangiosarcoma in the different organs was of capillary type.



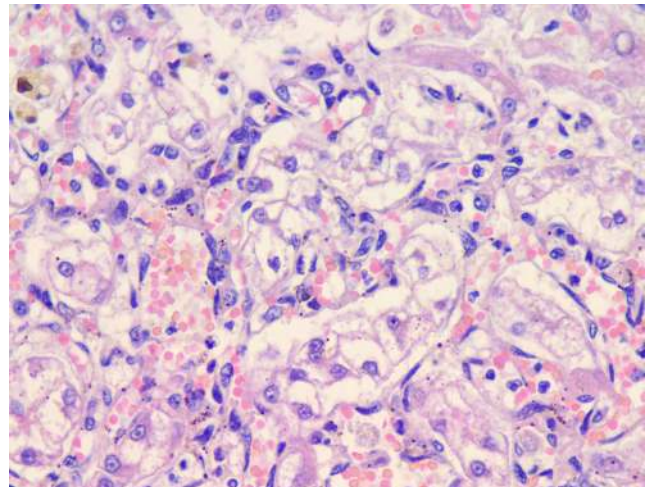
**Figure 4.** Spleen. Proliferated tumor cells forming blood vessels. H&E. x100.



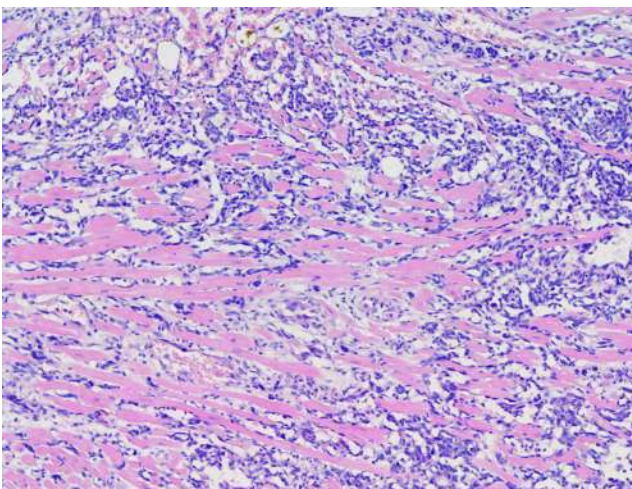
**Figure 5.** Spleen. High magnified Figure 4. Formation of capillaries by tumor cells. H&E. x400.



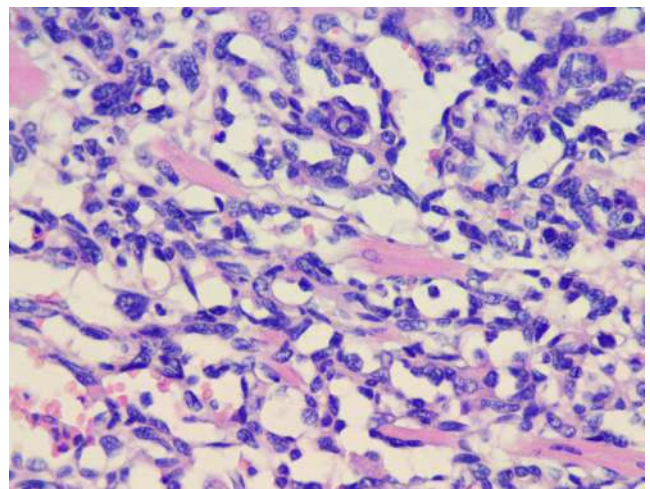
**Figure 6.** Liver. Proliferated tumor cells pressing the surrounding hepatocytes. H&E. x100.



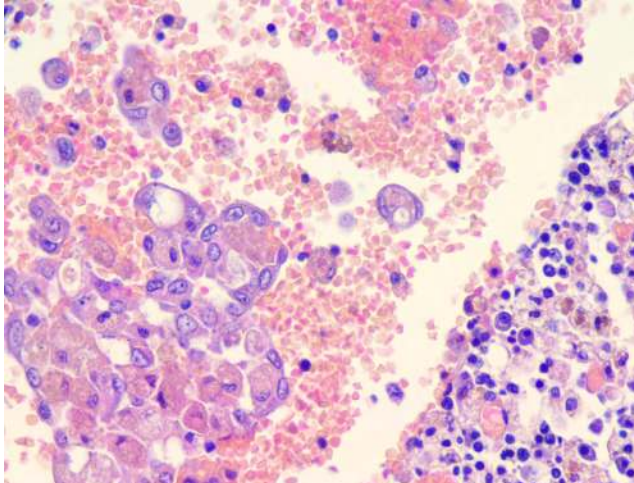
**Figure 7.** Liver. High magnified Figure 6. Proliferation of tumor cells in sinusoids. H&E. x400.



**Figure 8.** Heart. Invaded tumor cells between myocardial fibers. H&E. x400.



**Figure 9.** Heart. High magnified Figure 8. Proliferated tumor cells with atrophy of myofibers. H&E. x400.



**Figure 10.** Mediastinal lymph nodes. Tumor cells forming capillaries in the sinus. H&E. x400.

## Discussion

At first examination at the Veterinary Hospital of the Veterinary Faculty, Universidad de la República (Montevideo, Uruguay), nodules were already observed in multiple abdominal organs by ultrasonography. Histologically, although tumor cells were unequivocally detected in the spleen, liver, heart and various lymph nodes, it was difficult to determine the primary site of the tumor due to the lack registry of time-dependent clinical findings. However, it is presumed that the spleen was the primary tumor organ because of the higher number and size of tumors. Besides, the hemangiosarcoma is characteristic of this organ. If the spleen was the primary organ of the tumor in our study case, the tumors observed in the liver and heart have to be considered as metastatic lesions. It has been previously reported that canine hemangiosarcomas occur frequently in the spleen, and that this tumor is present in about 20-40% of splenic abnormalities (3, 6). In addition, more than 80% of splenic abnormal masses have been described as hemangiosarcomas (13). This tumor was reported to frequently metastasize the liver (2, 4, 8, 10, 14-16, 18), and it was also confirmed that more than 25% of splenic angiosarcomas metastasize the heart (2). Based on these reports and the present pathological findings, it is strongly possible that in our case the hemangiosarcoma first developed in the spleen, and then metastasized the liver and heart. Recently, an interesting clinical study reported the metastatic behavior of splenic hemangiosarcomas. As a result of a clinical follow-up of 34 large dogs treated with splenectomy due to splenic hemangiosarcoma, it was confirmed that metastases were found in the the following anatomical distribution: abdominal organs (including liver, kidney, omentum, and lymph nodes; n = 23), liver (n = 5), lungs and abdominal organs (including liver, kidney, omentum, and lymph nodes; n = 2), right cardiac atrium (n = 4), muscles (n = 2), lungs (n = 1), and subcutaneous flank

area (n = 1) (14). On the other hand, it was reported that most of the hemangiosarcomas present in the heart metastasize the lungs, and also muscles (1, 15). However, in this case, no metastases to lung or muscle were observed. Besides, the fact that tumor cell infiltration was characteristic in the sinuses of each lymph node, suggests that the metastases detected in different organs were mainly disseminated by lymphatic vessels.

Hemangiosarcomas are usually subdivided into various types of growth patterns (5, 7, 12, 17). In this study, an interesting feature is that the hemangiosarcoma found in all organs was the capillary type.

## Acknowledgements

The authors thank Dr. Claudio Borteiro for critically reviewing and English editing. Belén Varela and Camila Larrañaga are MSc students of Postgraduate Program of Facultad de Veterinaria, Universidad de la República. Belén Varela is fellowship recipient of Comisión de Investigación y Desarrollo Científico (CIDEDEC-FVET, Udelar, Uruguay). Camila Larrañaga is fellowship recipient of Agencia Nacional de Investigación e Innovación (POS-FMV-2020-1-1010108). Kanji Yamasaki is supported by Programa de Contratación de Investigadores Provenientes del Exterior (CSIC-Udelar, Uruguay), José Manuel Verdes acknowledge to CSIC-Udelar, PEDECIBA, and ANII (Uruguay).

## References

1. Carloni A, Terragni R, Morselli-Labate AM, Paninarova M, Graham J, Valenti P, Alberti M, Albarello G, Millanta F, Vignoli M. Prevalence, distribution, and clinical characteristics of hemangiosarcoma-associated skeletal muscle metastases in 61 dogs: A whole body computed tomographic study. *J Vet Intern Med.* 2019;33:812-9.
2. Clifford CA, Mackin AJ, Henry CJ. Treatment of canine hemangiosarcoma: 2000 and Beyond. *J Vet Intern Med.* 2000;14:479-85.
3. Day MJ, Lucke VM, Pearson H. A review of pathological diagnoses made from 87 canine splenic biopsies. *J Small Anim Prac.* 1995;36:426-33.
4. DeSandre-Robinson DM, Mariana T, Quina MT, David M, Lurie DM. Pericardial hemangiosarcoma in a 10-year-old Papillon. *J Am Anim Hosp Assoc.* 2018;54:e54504.
5. Dickerson EB, Thomas R, Fosmire SP, Lamerato-Kozicki AR, Bianco SR, Wojcieszyn JW, Breen M, Helfand SC, Modiano JF. Mutations of phosphatase and tensin homolog deleted from chromosome 10 in canine hemangiosarcoma. *Vet Pathol.* 2005;42:618-32.
6. Fernandez S, Lang JM, Maritato KC. Evaluation of nodular splenic lesions in 370 small-breed dogs (<15 kg). *J Am Anim Hosp Assoc.* 2019;55:201-9.

7. Gorden BH, Kim JH, Sarver AL, Frantz AM, Breen M, Lindblad-Toh K, Timothy D. O'Brien TD, Sharkey LC, Modiano JF, Dickerson EB. Identification of three molecular and functional subtypes in canine hemangiosarcoma through gene expression profiling and progenitor cell characterization. *Am J Pathol.* 2014;184:985-95.
8. Guinan J, Fischetti A, Garate AP, Chalhoub S. Primary peri-aortic hemangiosarcoma in a dog. *Can Vet J.* 2012;53:1214-8.
9. Hendrick, MJ. Mesenchymal Tumors of the Skin and Soft Tissues. In: Meuten, DJ. editor. *Tumors in Domestic Animals.* 5th ed., Iowa: Wiley Blackwell; 2017. p.142-75.
10. Iwata M, Aikawa T, Miyazaki Y, Sadahiro S. Primary colonic hemangiosarcoma in a dog. *Can Vet J.* 2018;59:373-8.
11. Johnson KA, Powers BE, Withrow SJ, Sheetz MJ, Curtis CR, Wrigley RH. Splenomegaly in dogs. Predictors of neoplasia and survival after splenectomy. *J Vet Intern Med.* 1989; 3:160-6.
12. Kim JH, Graef AJ, Dickerson EB, Modiano JF. Pathobiology of hemangiosarcoma in dogs: Research advances and future perspectives. *Vet Sci.* 2015;2:388-405.
13. Leyva FJ, Loughin CA, Dewey CW, Marino DJ, Akerman M, Lesser ML. Histopathologic characteristics of biopsies from dogs undergoing surgery with concurrent gross splenic and hepatic masses: 125 cases (2012–2016). *BMC Res Notes.* 2018;11:12.
14. Story AL, Wavreille V, Abrams B, Egan A, Cray M, Laura Selmic LE. Outcomes of 43 small breed dogs treated for splenic Hemangiosarcoma. *Vet Surg.* 2020;49:1154-63.
15. Yamamoto S, Hoshi K, Hirakawa A, Chimura S, Kobayashi M, Machida N. Epidemiological, clinical and pathological features of primary cardiac hemangiosarcoma in dogs: A review of 51 cases. *J Vet Med Sci.* 2013;75:1433-41.
16. Yoo S, Kim J, Myung HW, Woo S, Chung DJ, Lee AJ, Kim HJ, Do SH, Kim HY. Primary intrapelvic hemangiosarcoma in a dog. *J Vet Med Sci.* 2016;79:192-6.
17. Valli VE, Bienzle D, Meuten DJ. Tumors of the hemolymphatic system. In: Meuten, DJ. editor. *Tumors in Domestic Animals.* 5th ed., Iowa: Wiley Blackwell; 2017. p.209-321.
18. Verbeke F, Binst D, Stegen L, Waelbers T, de Rooster H, Goethem BV. Total venous inflow occlusion and pericardial auto-graft reconstruction for right atrial hemangiosarcoma resection in a dog. *Can Vet J.* 2012;53:1114-8.