

Solid Clear Cell Thymoma Associated with Hydropericardium in a Labrador Retriever

Ana Vitória Alves-Sobrinho¹, Bruna Samara Alves-Ribeiro¹, Lizandra Fernandes da Silva¹,
Andréia Vitor Couto do Amaral², Henrique Trevizoli Ferraz¹, Dyomar Toledo Lopes¹,
Klaus Casaro Saturnino^{1,2} & Dirceu Guilherme de Souza Ramos^{1,2}

ABSTRACT

Background: Thymoma is an uncommon neoplasm of thymic cells that is mostly benign and limited to the mediastinum region. Despite their sporadic occurrence in animals, thymomas are the tumors that most affect the anterior mediastinum of dogs. Reports of thymomas are scarce, however, despite their sporadic occurrence in animals, thymomas are the tumors that most affect the anterior mediastinum of dogs. This study reports a benign solid clear cell thymoma associated with hydropericardium as the cause of death in a Labrador retriever.

Case: One bitch presented with a history of hematemesis and hematochezia, obesity, dyspnea, bradycardia, anemia, neutrophilia, and increased liver enzymes and urea and creatinine metabolites. The hospitalization was carried out to carry out clinical examinations, but the patient died hours after admission. Necropsy revealed a pericardial sac that was severely distended with fluid, indicating the presence of hydropericardium. A firm rounded mass was observed in the mediastinum. Multiple organ fragments, nodules, and mediastinal mass were collected for microscopic evaluation. The mediastinal mass consisted mainly of solid neoplastic tissue of an epithelioid nature and lymphocytes. Other organs were normal. Lymphoid follicles and Hassall bodies were also observed, and the definitive diagnosis of benign solid clear cell thymoma associated with hydropericardium was confirmed. Despite clinical efforts and the availability investigative resources, the definitive diagnosis was only possible by necropsy due to the rapid evolution to death. The results were conclusive for the definitive diagnosis of benign solid clear cell thymoma associated with hydropericardium as the cause of death.

Discussion: Compared to other neoplasms, thymoma is relatively rare. In dogs, there are few reports of proven true thymomas, most of which are benign and do not metastasize. The morphological appearance of canine thymomas, as well as size and weight, is substantially diverse. In agreement with the present report, findings in the literature report staining of thymic epithelial tumors in varying shades of pink to yellowish white, with additional sections of beige, brown, white, and red. Most canine thymomas have cysts filled with serous or serosanguineous fluid, which we also observed in this case. The solid cellular arrangement belongs to predominantly epithelial thymomas, which can also show other cellular patterns, such as trabecular, cribriform, spiral or rosette-shaped. An uncommon epithelial variant, however, is the clear cell thymoma. In this type of tumor, large round epithelial cells are visible with abundant clear cytoplasm, variably indistinct cytoplasmic margins, and often containing a single prominent nucleolus, as depicted in the present report. Hassall corpuscles are considered useful diagnostic features, as they recapitulate the medullary portion of the normal thymus. Benign thymomas can lead to death due to compression of adjacent structures. The diagnosis of thymoma during the initial phase of the disease is extremely difficult, and ultrasonography and radiographic examinations are useful in detecting cranial mediastinal tumors. In this case, the tumor mass may have caused cardiac tamponade, thereby affecting systemic circulation, especially of the precardium, thus increasing hydrostatic pressure and resulting in fatal hydropericardium, before a possible diagnosis.

Keywords: canine, epithelial, Hassall's corpuscles, histopathology, necropsy, neoplasms, thymus, tumor.

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¹Laboratório de Patologia e Parasitologia Veterinária & ²Programa de Pós-Graduação em Biociência Animal, Instituto de Ciências Agrárias, Universidade Federal de Jataí (UFJ), Jataí, GO, Brazil. CORRESPONDENCE: D.G.S. Ramos [dguilherme@ufj.edu.br]. Medicina Veterinária, CIAGRA - UFJ. Campus Jatobá. BR 364, km 195, nº 3800. CEP 75801-615 Jataí, GO, Brazil.

INTRODUCTION

Thymoma is an uncommon neoplasm of thymic epithelial cells usually concomitant with varying degrees of lymphocytic infiltration in both humans and animals [7]. Most thymomas are benign and are usually confined to the mediastinum region. Thymomas exert pressure on adjacent tissues as they grow, and have a slow development and a late manifestation of clinical signs [9]. Less than a 3rd of cases are metastatic, or malignant when locally invasive, and reports of distant metastases are rare [11]. Despite their sporadic occurrence in animals, thymomas are the tumors that most affect the anterior mediastinum of dogs [23].

In human medical literature, many histological classification schemes for thymomas have been recommended in an effort to standardize criteria of clinical and prognostic significance [1]. Accordingly, the classification adopted in veterinary medicine is based on the density of preponderant cell populations. Three histological subtypes of thymoma were identified in animals: predominantly lymphocytic, predominantly epithelial, and intermediate (mixed) lymphoepithelial [1,4].

In the present report, we provide anatomopathological descriptions of a benign solid clear cell thymoma associated with hydropericardium as the cause of death in a Labrador retriever.

CASE

A 6-year-old bitch Labrador retriever weighing 46 kg was presented for a new medical evaluation 14 days after hematemesis and hematochezia. Previous ultrasound examination indicated the presence of free fluid in the thoracic and abdominal cavities. The last deworming record was dated 3 weeks before the appointment and the vaccination protocols were conducted according to World Small Animal Veterinary Association (WSAVA) Guidelines [6].

Physical examination revealed depression, obesity, severe dyspnea, bradycardia, emesis, and slightly pale mucous membranes. Maropitant Citrate¹ [0.1 mg/kg, SC] was administered to control vomiting. The diagnostic suspicions focused mainly on neoplasms, diabetes, and liver diseases, due to the similarity of clinical findings, but heart disease and pneumonia were not ruled out owing to the bradycardia and dyspnea.

Blood samples were collected, and complete blood count assessment revealed normocytic and

normochromic anemia accompanied by neutrophilia. Levels of alanine aminotransferase (141 UI/L), alkaline phosphatase (882 UI/L), creatinine (2.4 mg/dL) and urea (110.6 mg/dL) metabolites were increased, although the albumin (3.03 g/dL) level was normal.

The hospitalization was carried out to carry out clinical examinations. However, the patient died hours after admission and a necropsy was performed, and the external aspects revealed an above-normal body condition. No changes were observed in the trachea. A small amount of citrine fluid was present in the thorax. The lungs, in their extension, showed a partially reddish color, characteristic of mild congestion. The pericardial sac was severely distended, and a large amount of non-coagulated dark red fluid was observed, indicating the presence of hydropericardium. In the heart, whitish clumps were observed adhered to the cardiac tissue.

In the anterior mediastinum, a firm rounded mass was observed (Figure 1), with a very light pink color, delimited contours, measuring approximately 3.63 x 3.84 x 2.85 cm, and weakly adhered to the adjacent tissues. Other masses located close to the vessels of the heart base with perceptible delimitation, light pink coloration, and interspersed fatty tissue were also observed.

The centrilobular zone of the liver contained hepatocytes with altered cytoplasm and nucleus, which is characteristic of diffuse centrilobular necrosis. The spleen showed segmental areas with accumulation of red blood cells which were classified as a segmental hemorrhagic splenic infarction.

Other organs were normal. Multiple organ fragments, nodules, and mediastinal mass were collected for microscopic evaluation. Samples were fixed in 10% buffered formalin, embedded in paraffin wax, sectioned, and stained with hematoxylin² and eosin³ (HE) prior to brightfield microscopic examination (Nikkon Eclipse E200⁴).

The mediastinal mass consisted mainly of solid neoplastic tissue of an epithelioid nature. Interspersed cells with scant cytoplasm and heterogeneous round nuclei representing infiltrating lymphocytes were also observed. Neoplastic epithelial cells had ill-defined cytoplasmic margins and significantly large, pale, vesicular nuclei, with one or, sporadically, two prominent nucleoli. Multifocally, lymphoid follicles and Hassall bodies (groups of concentric epithelial cells with eosinophilic cytoplasm) were also observed (Figure 1).

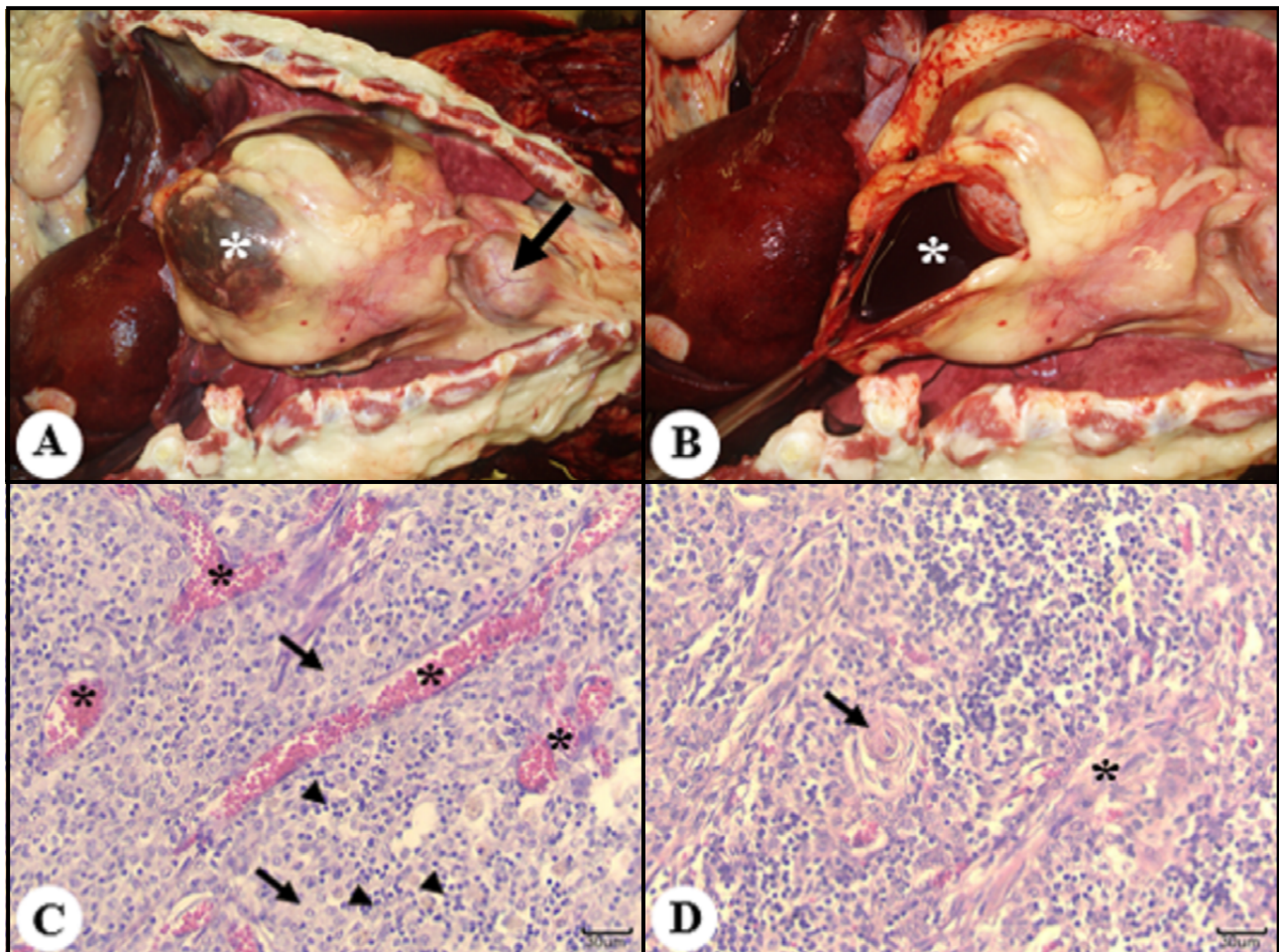


Figure 1. Anatomopathological examination of a dog with thymoma. A- Image of the open chest, after sternal plastrum retraction, demonstrating a neoplastic thymoma mass (arrow) in the precardiac mediastinum, in addition to diffuse and severe hydropericardium (*). B- Same image as A, but with an open pericardial sac, demonstrating the amount of fluid within, justifying cardiac tamponade. C- Microscopic image of the tumor, demonstrating neoplastic cells (arrows), high vascularization (*) and few lymphocytes (arrowhead). [HE; 20x. Bar= 30 µm]. D- Microscopic image of the same tumor, demonstrating the presence of Hassall's bodies (arrow), confirming thymoma (arrow). Note thin conjunctival trabeculae supporting the neoplastic parenchyma (*). [HE; 20x. Bar= 30 µm].

The results were conclusive for the definitive diagnosis of benign solid clear cell thymoma associated with hydropericardium as the cause of death.

DISCUSSION

Compared to other neoplasms, thymoma is relatively rare, as indicated by the lack of large studies and case descriptions in the literature [19,23]. In dogs, there are few reports of proven true thymomas, most of which are benign and do not metastasize [3,8,25]. Some studies of single cases involving malignant metastatic thymomas in dogs have been previously reported [16,24]. Other domestic species that are reported to develop sporadic thymomas include cats [22], large ruminants [7], rabbits [13], goats [4,9], and pigs and sheep [21].

The morphological appearance of canine thymomas, as well as size and weight, is substantially

diverse [2]. In agreement with the present report, findings in the literature report staining of thymic epithelial tumors in varying shades of pink to yellowish white, with additional sections of beige, brown, white, and red [15,16]. Most canine thymomas have cysts filled with serous or serosanguineous fluid, which we also observed in this case [2]. There are several explanations for the appearance of cysts in thymomas, with cystic degeneration being the most frequent peculiarity. Cysts may also represent dilatations of fused lymphatic cavities or perivascular spaces in which central vessels have disappeared [5,18]. Thymomas with cystic qualities must be distinguished multilocular thymic cysts. Thymic carcinomas with cystic changes should also be considered. In such cases, several sections may be necessary for a correct diagnosis [7].

The thymoma of the present case, classified microscopically as a solid clear cell tumor, is similar

to the thymic epithelial tumors described in animals [15,17]. The solid cellular arrangement belongs to predominantly epithelial thymomas, which can also show other cellular patterns, such as trabecular, cribriform, spiral or rosette-shaped [7]. The predominantly epithelial type corresponds to most thymomas in animals, and shows a range of histological features similar to thymic tumors in humans [14]. An uncommon epithelial variant, however, is the clear cell thymoma. In this type of tumor, large round epithelial cells are visible with abundant clear cytoplasm, variably indistinct cytoplasmic margins, and often containing a single prominent nucleolus, as depicted in the present report [15]. Clear cell thymomas are more frequent in dogs than in humans, where they are particularly uncommon [15].

Hassall corpuscles are considered useful diagnostic features, as they recapitulate the medullary portion of the normal thymus. When present in large numbers, Hassall bodies are usually indicative of pre-existing structures surrounded by a neoplasm other than thymoma. The lymphoid follicles identified by microscopy are elements that may be particularly present in canine thymomas. Additionally, thymomas may also contain infiltrations of mast cells, eosinophils, macrophages, melanocytes, plasma cells, and neutrophils in varying amounts, which were absent in this case [7,11].

As in humans, the best indication of thymoma malignancy is the behavior presented by the tumor,

such as invasiveness, vascular infiltration, and occurrence of metastases [16]. The tumor observed in this study was well delimited and contained by the thymic capsule, which also indicated benignity, and evolved by expansion rather than infiltration as described for benign thymomas [2,10,12]. However, benign thymomas can lead to death due to compression of adjacent structures. In this case, the tumor mass may have caused cardiac tamponade, thereby affecting systemic circulation, especially of the precardium, thus increasing hydrostatic pressure and resulting in fatal hydropericardium.

The diagnosis of thymoma during the initial phase of the disease is extremely difficult [20]. Ultrasonography and radiographic examinations are useful in detecting cranial mediastinal tumors [4,9,19,25]. In summary, despite clinical efforts and the availability of investigative resources, definitive diagnosis was only possible by necropsy, as is often the case in veterinary medicine [4,7].

MANUFACTURERS

¹Zoetis Indústria de Produtos Veterinários Ltda. Campinas, SP, Brazil.

²Wcor Corantes e Soluções Ltda. São Paulo, SP, Brazil.

³Vetec Química Fina Ltda. Rio de Janeiro, RJ, Brazil.

⁴Nikkon Instruments Inc. Melville, NY, USA.

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