



### Case report

## Mixed thymoma in a German Shepherd dog

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### Abstract

A thoracic neoplastic mass in a 6 years-old German Shepherd dog was examined. The dog had apathy, regurgitation, and ascites. A large mass occupying the cranioventral, medial and caudal mediastinum was found by X ray and ultrasonography. Grossly, a 27 x 23 x 12 cm encapsulated, multilobulated, and cystic mass was found. Firms adhesions were present between the neoplasm and the right and left cranial lung lobes. Histopathologically, the neoplastic cell population consisted of solids sheets of epithelial cells and aggregates or individual lymphocytes. By immunohistochemistry, proliferating epithelial cells were positive for keratin and lymphocytes were intensely positive for CD3, identifying them as T cells. Based on gross, histologic, and immunohistochemical findings, the neoplasm was diagnosed as a mixed thymoma.

**Key Words:** Canine, thoracic neoplasia, thymoma, lymphocytes T, immunohistochemistry.

### Introduction

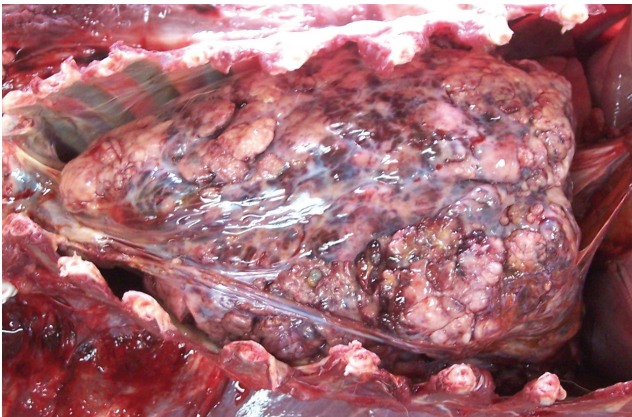
The thymus is a lymphoepithelial organ, which a major site for development and differentiation of T cells. The thymus atrophies after puberty, but remnants can undergo neoplastic proliferations (1, 11). Thymomas are neoplasm of thymic epithelium in which there are various degrees of benign lymphocytic infiltration (17). Thymomas seem to occur at a relatively high prevalence in cats and dairy goats but in other animal species they are considered uncommon (8, 9, 15). These tumors are typically slow-growing, noninvasive, and rarely metastasize (5, 11, 13). Most are benign, but malignant thymomas have also been reported in animals (2, 4). In human medicine, classification schemes attempt to establish criteria of clinical and prognostic significance.

Histologic and immunophenotypic resemblance to cortical or medullary thymic regions, and the relative number of epithelial cells and lymphocytes are the main features for classifying thymomas (5, 16). In veterinary medicine, classification is based only on density of lymphocytes within the neoplasm, resulting in three histologic subtypes: epithelial predominant, lymphocyte predominant, or mixed type (9, 18). Animals with thymomas are most often presented as a result of clinical sings related to a space-occupying cranial mediastinal mass (4), and some are associated with acquired myasthenia gravis and megaesophagus (1, 10).

### Case report

A 6-years-old, female, German Shepherd dog was presented to the Veterinary Hospital of the National University of Asunción (FCV-UNA) on July 2007, with clinical signs of weakness, apathy, regurgitation, and ascites. Clinically, the dog had emaciation. The respiratory rate was 35 movements/min, with superficial respiratory movements. The heart rate was 88 beats/min, strong and rhythmic. Body temperature was 38.2 °C. Ultrasonography demonstrated fluid within the abdominal cavity, and a heterogeneous mass with hypoechoic and anechoic pockets, occupying the ventral area of the thoracic cavity, caudally displacing the heart. X ray revealed intense radio opacity on cranial, medium and caudal mediastinal areas. Due to poor prognosis, euthanasia was elected, and the dog was submitted for necropsy at the Veterinary Pathology Department of the Facultad de Ciencias Veterinarias, National University of Asunción.

Grossly, a 27 x 23 x 12cm encapsulated, multilobulated mass occupying the cranioventral, medial and caudal mediastinum was observed within the thoracic cavity. The neoplasm was displacing the heart, and dorsal and caudal lung lobes, (Fig. 1). The mass was firmly adhered to right and left cranial lung lobes with no apparent invasion of the pulmonary parenchyma. The surface of this mass was white to gray with some hemorrhagic necrotic areas. On cut surface, multiple lobes of homogeneous firm, white to gray tissue separated by incompletely fibrous septa was evident. Many cystic cavities with thin walls, filled with yellowish fluid were also observed within the neoplastic tissue.

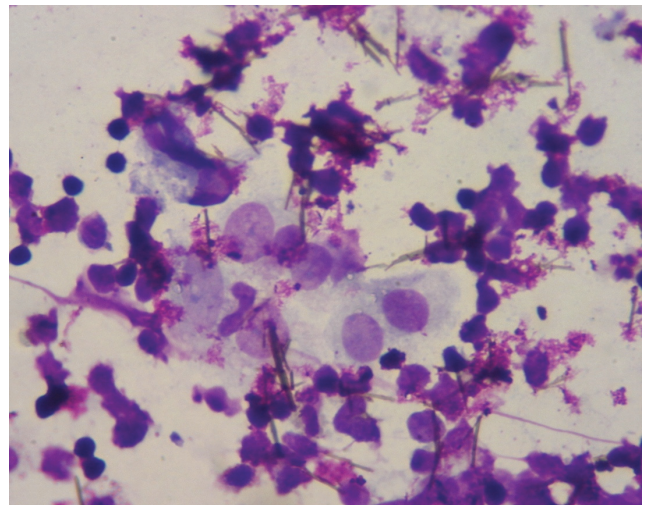


**Fig. 1** German shepherd dog. Thoracic cavity. A 27x 23x 12 cm. multilobulated and encapsulated mass occupying the cranioventral, medial and caudal mediastinum.

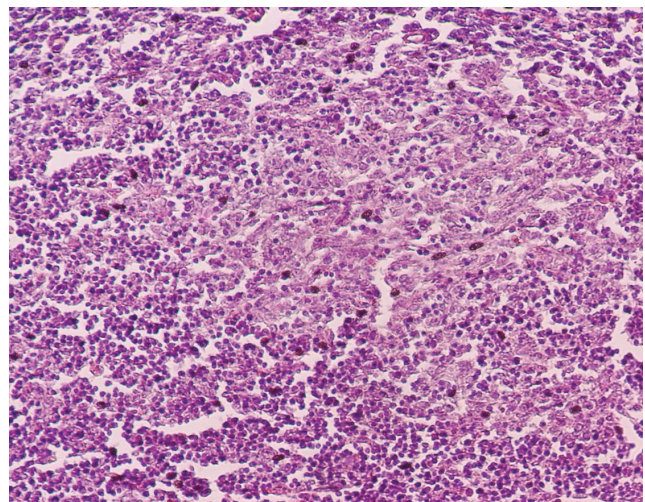
Small well differentiated lymphocytes were observed in cytological smears. Polygonal cells with large pale grey-blue cytoplasm, round to oval eccentrically nuclei with fine chromatin patterns and one or two evident nucleoli were seen in small clumps. A few mast cells were also present (Fig. 2)

Histologically, the neoplasm was composed of a heterogeneous population of smalls well differentiated lymphocytes as individualized cells or in small clusters;

trabecular and solid sheets of polygonal epithelial cells. The polygonal cells had indistinct borders, large, pale grey-blue cytoplasm and round to oval nuclei with finely stippled chromatin and one or two nucleoli. (Fig 3). In some areas, cells with strong eosinophilic cytoplasm formed concentric clusters compatible with Hassal's bodies. Cystic cavities were lined by a single layer of nonciliated epithelium. Incomplete bands of fibrovascular tissue give the multilobulated pattern of the neoplasm. Immunohistochemically, monoclonal mouse anti-human cytokeratin (cytokeratin AE1/AE3, DakoCytomation, USA) was used as primary antibody, and reveled with LSAB-HRP (Dako, USA). Lymphocytes were intensely positive for Polyclonal rabbit anti-human CD3 (DakoCytomation, USA), confirming T-cell origin (Fig. 4 and 5).



**Fig. 2** Mixed thymoma; dog. Cytological imprint. Polygonal epithelial-like cells with large pale grey-blue cytoplasm and small lymphocytes. Giemsa x100.



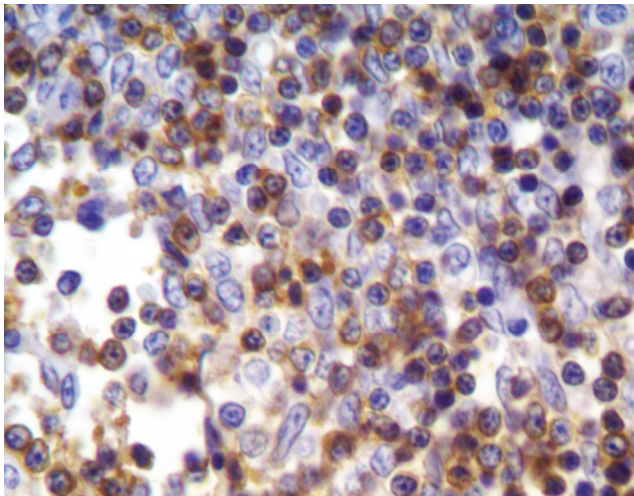
**Fig. 3** Mixed thymoma; dog. Polygonal cells and small lymphocytes. H & E. x40.



## Discussion

Thymomas are uncommon tumors in dogs. It occurs more frequently in adult or older dogs and in Labradors and German Shepherd dogs (6). The cranioventral mediastinum is their usual site of occurrence but they can also be present in cervical region and caudal mediastinum. Grossly, they appear as a soft or firm, white to grey, multilobulated mass that often cannot be distinguished from mediastinal lymphosarcoma, and histopathologic and/or immunohistochemistry are necessary to determinate the origin of the neoplasm. Although lymphosarcoma are more frequent in young dogs (6, 9).

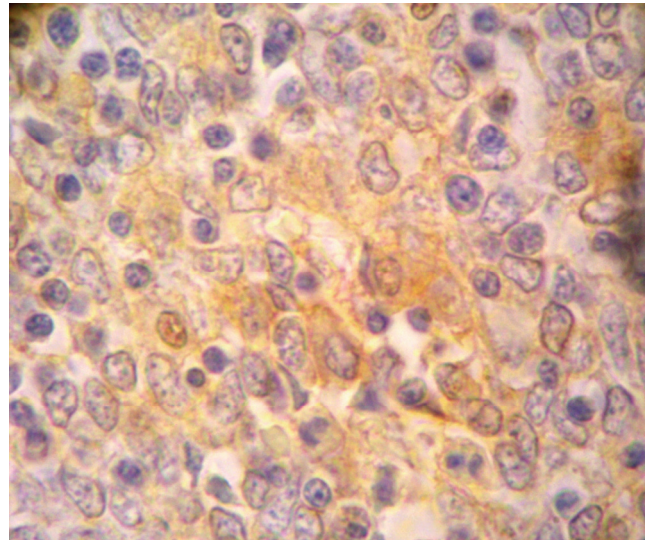
Cystic changes are another common gross feature of thymomas, consisting in multiple cavities filled with yellowish fluid as observed in this case. These cysts might represent cystic degeneration. Another possibility is that they represent pseudocysts originating from invaginations of the surface-lining mesothelium. They have also been considered to be dilated and fused lymph cavities or perivascular spaces in which the central vessels have disappeared (14, 18, 19). Conversely, brachial cleft, thymic, bronchial and esophageal cysts may appear in the cranial mediastinal area and most of them are originated from the endoderm of the 3<sup>rd</sup> and 4<sup>th</sup> pharyngeal pouches. They are classified according to their morphological features of the cyst wall and location. There are a few case reports of human and dogs thymomas arising in the wall of these thymic cyst (3, 10, 12), which are distinguished from cystic changes of thymomas.



**Fig. 4** Mixed thymoma; dog. CD3 positive lymphocytes. LSAB-HRP method. x100.

There is a relatively good correlation between the cytological and histopathological features in thymomas. Discrepancies are the detection of a greater number of epithelial-predominant histologically and a failure to recognize Hassal's corpuscles cytologically (4). In this particular case, cytological smears demonstrated a bimorphic population of cells consisting of moderate

amount of polygonal and spindle-shaped epithelial-like cells and greater amount of small lymphocytes. Hassal's corpuscle was not recognized cytologically. Histologically, both types, epithelial cells and lymphocytes, were present in the same proportion. Lymphoid component of thymomas exfoliates more readily, either by aspiration or imprint techniques, than the epithelial component because epithelial cells are more firmly anchored to the structural framework of the tumor. For whatever reason, the architecture of Hassal's corpuscles is not retained in cytological preparation and therefore it is not a useful cytological criterion (4).



**Fig. 5** Mixed thymoma; dog. AE1/AE3 (pan-cytokeratin) positive cells. LSAB-HRP method. x100.

The epithelial cells can be arranged in different patterns including solid, trabecular, cribriform, whorled, or roset-like (9). In this case trabecular and solid sheets of polygonal cells were observed. A few concentric clusters of epithelial cells with strong eosinophilic cytoplasm resemble Hassal's bodies; they are usually considered to be helpful diagnostic features of the tumor because they recapitulate the medullary portion of the normal thymus. Lymphocytes were present individually and in small clumps. The proportion of neoplastic epithelial cells and nonneoplastic lymphocytes varies widely between tumors and between different lobules of the same tumor (2, 4, 9, 14). Immunohistochemical markers can be used to differentiate the epithelial cells and lymphocytes, aside from the proportion of both cell types (7, 16). Lymphocytes were strong positive for CD3 confirming that this population of lymphocytic cells was composed mostly of T-cells. The epithelial cells were positive for keratin making no distinction of cortical and medullary epithelial type. Cytokeratin cocktail was not used as marker therefore we cannot establish the medullar or cortical origin of this thymoma. Based on the veterinary classification of thymomas (9, 18), this particular case is categorized as mixed type.

The majority of thymomas are benign. Local invasion and metastasis are considered to be uncommon. Metastasis can occur in the pulmonary and pericardial pleura, lungs, mediastinal lymph node, in the cranial thoracic aperture, kidneys and uterus (1, 9, 18). In the absence of any features of malignancy, this case is considered benign in nature.

The clinical signs associated with thymomas depend of the location of the mass and the compression of the different structures within the thoracic cavity (9). Ascites and regurgitation were present due to the compressive action of the mass on the greater vessels and thoracic portion of the esophagus respectively. No signs of acquired myasthenia gravis and megaesophagus were observed in this case.

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