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Case Report

Mixed Thymoma in a Goat

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Abstract

This article describes the gross, histopathological, and immunohistochemical findings of a mixed thymoma in a 2-year-old, mixed-breed, female goat. A large space-occupying neoplastic growth was observed within the cranial thoracic cavity, which by histology was well-encapsulated and formed by the proliferation of spindle-shaped epithelial cells arranged in solid sheets or rosette-like formations with varying accumulations of lymphocytes. Immunohistochemistry demonstrated that the neoplastic epithelial cells expressed cytokeratin, with negative immunoreactivity to vimentin, thyroglobulin, Chromogranin A, neuron-specific enolase, and glial fibrillary acidic protein. The lymphocytic population expressed CD3 and CD2. These findings favor a diagnosis of mixed thymoma.

Key Words: goat, thymoma, immunohistochemistry, pathology

Introduction

Thymomas are tumors derived from the epithelial components of the thymus that contain variable degrees of benign lymphoid proliferating cells (16). These tumors are considered rare in most species of animals (7, 10, 16), but an apparent elevated frequency has been described in a specific herd of Saanen dairy goats (6). In domestic animals, there are descriptions of this tumor in the goat (6, 9, 11), horse (5, 14, 17), dog (2, 10), cow (4, 10, 13), sheep (13), and cat (10).

However, since the initial reports of this tumor in goats (6, 9, 11), there has not being recent descriptions of its occurrence in this specie. It is unknown if the absence of recent descriptions is due to the low incidence of this tumor worldwide or simply because it has been termed frequent in goats (6); hence, there is no need to describe this lesion. This report describes the pathological and immunohistochemical findings of a thymoma in a goat.

Materials and methods

Animal description, necropsy, and histopathology

A 2-year-old, mixed-breed, female goat, with unknown clinical history, which originated from a public farm maintained by the City of Helsinki died suddenly. The animal was submitted for routine necropsy at the Section of Veterinary Pathology, University of Helsinki, Finland. Various tissue fragments from the tumorous growth and from selected organs (liver, spleen, kidney, lungs, and brain) were fixed in 10% neutral buffered formalin solution and routinely processed for histopathological evaluation.

Histochemistry and immunohistochemistry

Selected tissue sections were stained by the Periodic Acid Schiff (PAS) histochemical method, and replicate sections used for immunohistochemistry (IHC). IHC was done by using the streptavidin-biotin technique in an automated staining system (LabVision, California, USA). The panel of primary antibodies included reagents specific for glial fibrillary acidic protein, GFAP (Serotec, Oxford, UK), neuron-specific enolase, NSE (Serotec), thyroglobulin (Serotec), Chromogranin A, ChA (Serotec); vimentin (DAKO, Carpentaria, CA, USA), CD 2 (DAKO), CD 3 (DAKO), and cytokeratin (DAKO). Positive and negative controls consisted of sections from normal goat thyroid, but for negative controls normal rabbit serum substituted the

primary antibody.

Results

Necropsy

The animal was of regular body condition with a severely enlarged thoracic cavity. Gross abnormalities were restricted to the thoracic cavity and the liver; significant pathological alterations were not found in other tissues and organs. There was a large (15 x 20 x 30 cm), firm, 7.1 kg, well-encapsulated, oval shaped neoplastic space-occupying growth within the cranial region of the thoracic cavity, which resulted in compressive atrophy to the adjacent lungs and dislocation of the heart (Fig. 1A). The tumorous growth was partially attached to the pericardial sack, the diaphragm, the diaphragmatic lobe of the lung, and the parietal pleura. The sectioned surface of the tumor was smooth, cream to white, with several ill-defined glandular-like structures, and one cystic cavity (5 cm in diameter) at the caudal extremity; the cyst contained a brown, foul smelling liquid (Fig. 1B). Further, there was moderate hydrothorax, ascites, pulmonary edema, marked accentuation of hepatic lobules with increased hepatic consistency. At this time the gross differential morphological diagnoses of the intrathoracic mass included ectopic thyroid adenoma, thymoma, and aortic body chemodectoma.

Histopathology

Significant histological alterations were restricted to the mass within the thoracic cavity, and to some extent the liver and lungs. Histopathology of the neoplastic mass revealed a well-encapsulated tumor that contained large areas of epithelial growth with several, randomly distributed, accumulations of lymphocytes, which in some areas interspersed the proliferated epithelial growth (Fig 2 A-B). The amount of epithelial relative to lymphocytic component of the lesion varied based on part of the tumor evaluated. Within areas of lymphocytes, there were sparse accumulations of concentrically arranged keratinized reticular cells (Fig. 2C), all of these structures observed were not well preserved. The epithelial component was formed by the proliferation of extensive mass of neoplastic cells which was subdivided by thin fibrous septa. Within this expansive mass, the tumor consisted of neoplastic cells arranged as solid masses and/or as rosette-like structures. Within these rosette-like formations, the neoplastic epithelial cells were elongated to spindle-shaped, randomly distributed, demonstrated discrete cellular and nuclear pleomorphism, and with indiscrete cellular borders (Fig. 2D). The cytoplasm of most epithelial cells within these rosette-like formations was finely vesicular; with centrally to paracentrally located nuclei and indistinct nucleoli; few mitotic figures were observed.

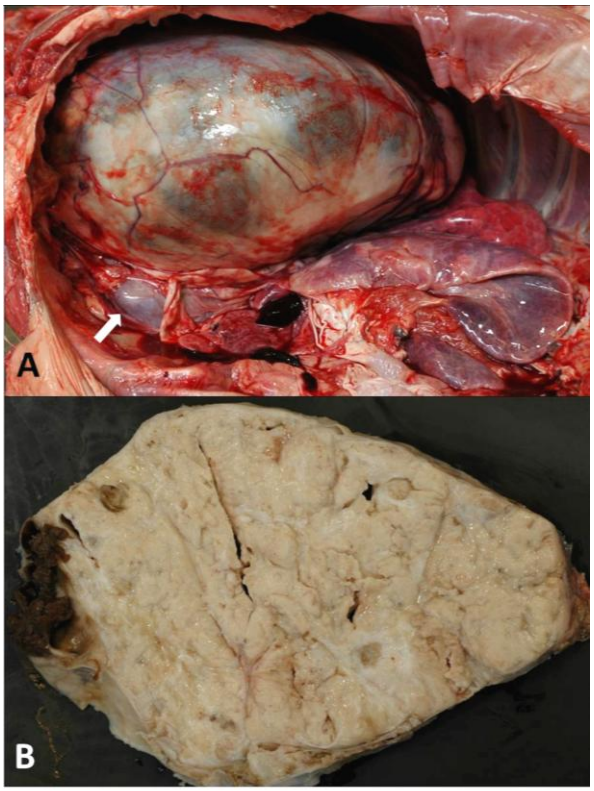

Figure 1. Gross characterization of thymic adenoma in a mixed-breed goat. There is a large, well-encapsulated, space-occupying tumor with the thoracic cavity; observe compressive atrophy of the lungs and the dislocated heart (arrow) (A). Sectioned surface of intrathoracic tumor; observe the glandular-like pattern and a cystic regions (B).

Additionally, there were several follicular-looking structures that were lined by a single layer of flattened epithelial cells (Fig. 3A) and contained an eosinophilic PAS-positive material (Fig. 3B), while others were severely dilated and were surrounded by ciliated columnar epithelial cells (Fig. 4A). The cytoplasm of the epithelial cells located adjacent to these dilated structures was either cloudy to finely vacuolated or contained remnant of fatty-looking droplets (Fig. 4B). Further, hemorrhage, inflammation, or necrosis was not observed within the tumorous growth. Pulmonary alterations included moderate congestion and edema, while hepatic lesions included severe portal and bridging fibrosis, moderate centrilobular necrosis, severe congestion of hepatic sinusoids, and discrete lipidosis.

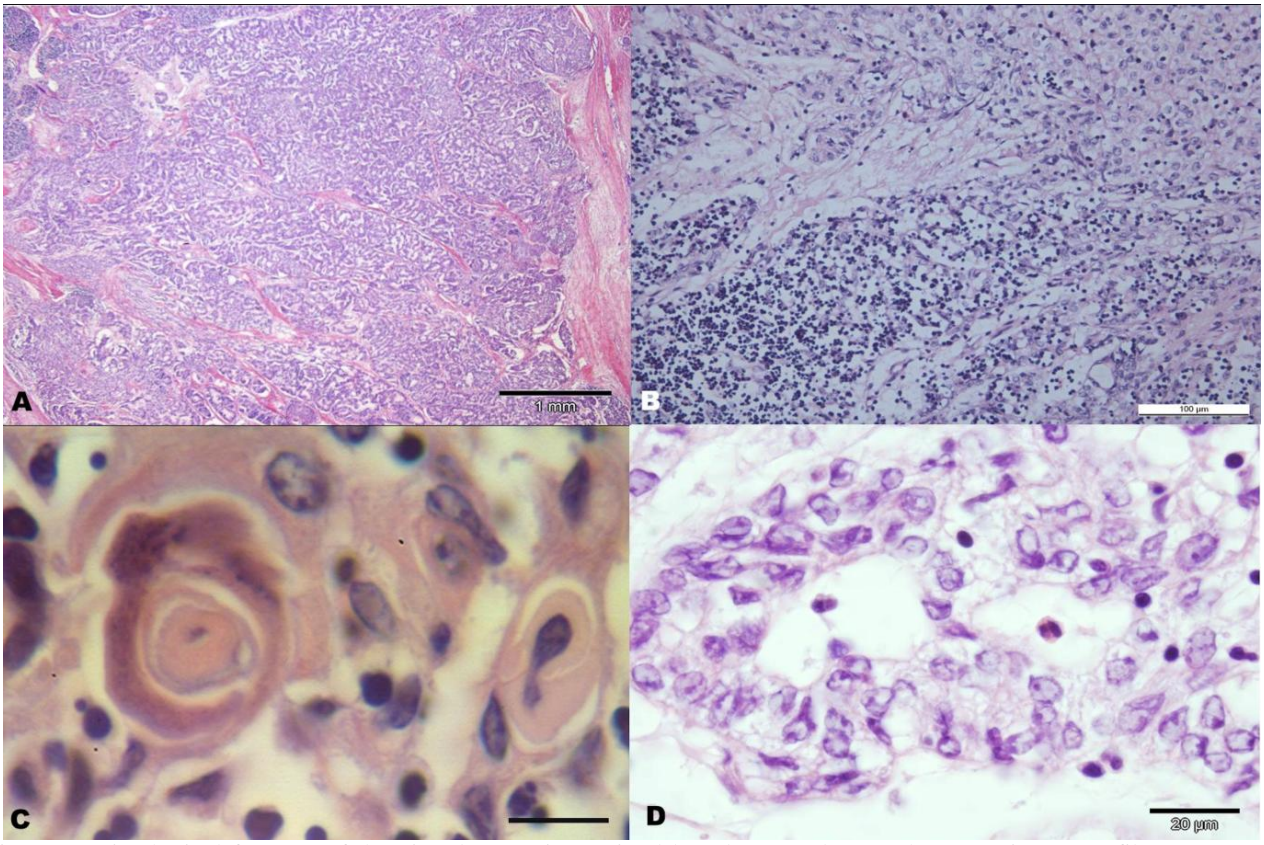

Figure 2. Histological features of thymic adenoma in a mixed-breed goat. Observe the extensive outer fibrous capsule and the proliferation of fibrous connective tissue within the mass forming sheets and cords of neoplastic epithelial cells (A), accumulation of lymphocytes within the neoplastic mass (B), and a characteristic Hassall corpuscle typical in the medullary region of the thymus (C). The elongated-spindle shaped, haphazardly distributed, epithelial cells with indistinct cellular borders are arranged in rosette-like formations (D). (Hematoxylin and Eosin; Bar: A, 1 mm; B, 100 µm; C and D, 20 µm).

Immunohistochemistry

The immunohistochemical reaction was uniform within all evaluated tissue sections. The neoplastic epithelial cells expressed cytokeratin (Fig. 5A) but were labeled negative for vimentin, thyroglobulin, ChA, and NSE, and GFAP. However, positive vimentin immunoreactivity was restricted to the fibrous connective tissue that surrounded the rosette- and follicular structures (Fig. 5B). In addition, the lymphocytic populations demonstrated intense positive immunoreactivity to CD 2 within the cortical (Fig. 6A), and to CD 3 at the medullary (Fig. 6B) regions of the neoplastic mass.

Discussion

The anatomic localization of the neoplastic mass, the histological features, and the immunohistochemical characteristics supports a diagnosis of mixed thymus adenoma (mixed thymoma); in veterinary pathology, thymomas are classified as predominantly epithelial or lymphocytic, or mixed (7, 16), based on the histological components of the tumor. The concentrically arranged keratinized reticular cells observed within accumulations of normal lymphocytes were interpreted to be Hassall's (thymic) corpuscle, which is a characteristic feature of the medullary region of the thymus (1, 15, 16). However, not all thymic corpuscles within the neoplastic growth were well-defined, and these were considered as abortive thymic capsules; similar findings were described in thymomas of the goat (9), horse (17), and cow (4). The strong cytokeratin immunoreactivity without expression of vimentin characterizes the proliferating neoplastic cells as of epithelial origin. Further, characterization of a primary thymic neoplastic mass rather than a tumor originating from the thyroid gland, chemoreceptor cells, or neurological origin, was obtained by the negative immunoreactivity of the proliferating epithelial cells to thyroglobulin, Chromogranin A, NSE, and GFAP; thereby eliminating chemodectoma and thyroid adenoma from the initial list of gross diagnoses.

Positive immunoreactivity of the lymphocytes to CD2 and CD3 confirmed their origin as T-lymphocytes. This difference in immunoreactivity of thymic lymphocytes is a direct manifestation of the encoding of the T-cell receptors during thymic morphogenesis, where the earliest development of T-cells occurs within the outer cortex with the expression of CD2, and as the lymphocytes matures they progressively express CD3+ antigen (16). The positive immunoreactivity to cytokeratin of the proliferating

epithelial cells and the demonstration of a T-cell origin of the lymphocytes, confirms the neoplastic lesion to be composed of two distinct cellular populations, and consequently should be characterized as mixed thymoma.

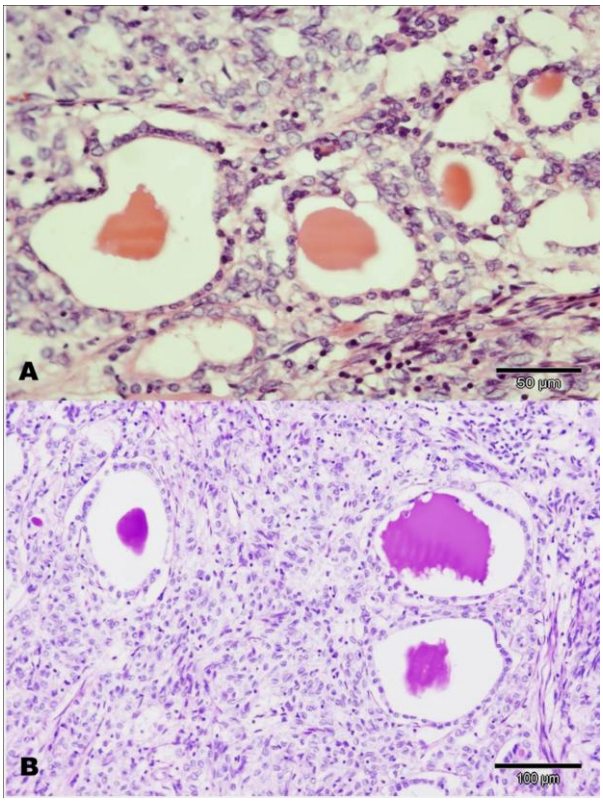

Figure 3. There are accumulations of follicular structures containing an eosinophilic colloid-like material within the tumor (A), which demonstrated a positive-Periodic Acid Schiff reaction (B). (Hematoxylin and Eosin; Bar, A 50 µm; B, 100 µm).

Unique to this tumor was the finding of islands of follicular-looking cells with a colloid-like PAS-positive material and cells demonstrating remnants of ciliated epithelia, while cells adjacent to these dilated structures were either finely vacuolated or seemed to have contained remnants of fat droplets. These vacuolated or lipid-filled cells were interpreted as being the inactive clear principal cells of the parathyroid gland which are known to contain glycogen and lipid droplets (12). Collectively, these histological features have been described within the parathyroid gland of the adult sheep and goat (1), and are frequently observed within the adult parathyroid of humans (15). Unlike most other domestic animals, the cortical region of the parathyroid gland of sheep and goats has been described as containing populations of clear principal cells, with their darker counterparts located at the medulla, while these cells are randomly interspaced in other domestic animals (1). These findings suggest that these structures might represent remnants of the cortical parathyroid. These pseudofollicles closely resemble the colloidal follicles of the thyroid gland, but their negative immunoreactivity to thyroglobulin, excluded the possibility of being of thyroidal origin. Further, no other naturally occurring organ/tissue with similar morphology is described as occurring next to or adjacent to the anatomic location of the neoplastic growth. Nevertheless, similar structures have not been described in most cases of thymic neoplasia in domestic animals (2, 4, 6, 10, 11, 13, 14), but are frequently characterized as developmental abnormalities in humans (12, 15). There is one mention of similar structure within a malignant thymoma of a horse (5), without additional details. These pseudofollicles of the parathyroid gland are derived from the proliferation of ischemic and degenerated parenchymal cells and the eosinophilic homogenous colloid-like secretion contain glycoproteins resulting in a PAS-positive reaction (12); resembling structures seen in this case. During embryogenesis part of the developing parathyroid gland (parathyroids III) originates from the dorsal part of the left and right third pharyngeal pouches, while the thymus originates from the ventral portion of the same embryonic structures (3, 8, 12). As maturation progresses, the parathyroids III are carried down the neck by the developing thymus (3), and are generally located close to the bifurcation of the carotid artery (8); one structure being distant from the other, but ectopic parathyroid is frequently observed in humans (12). Although it can be argued that these structures might have originated spontaneously within the neoplastic growth, the typical histological features that closely resembles remnants of the cortical parathyroid (1,12) associated with the close proximity of the thymus and parathyroid during embryonic development (3,8), support the hypothesis that these structures are most likely to be of parathyroidal origin. Consequently, the ectopic location of parathyroidal tissue within the thymus of this goat might suggest that there was no separation of the parathyroids III from the thymus during embryogenesis, implying that the neoplastic lesion might have occurred early in the formation of this goat, with continued growth during puberty and until the animal became matured.

Although thymomas are considered to be common neoplastic growths of a specific breed of dairy goats (6), there has been not any recent description of this tumor in this specie other than the early reports (6, 9, 11). Alternatively, there have been recent descriptions of thymomas in other species of domestic animals (2, 4, 5, 14). This absence of recent reports of cases of caprine thymomas might suggest either: a) there are comparatively reduced numbers of caprine necropsies done within most Veterinary Hospitals relative to other domestic animals; b) that the tumor is not frequently observed in goats from some geographical locations; c) that this neoplastic growth is common but underreported, because it was previously described as common in goats (6); or d) that the tumor might have been more prevalent in a specific breed of goats. This case might represent the first description of caprine thymoma from Northern Europe; alternatively, there is no reported description of thymomas in goats from Brazil, where large populations of goats are reared for milk and meat production.

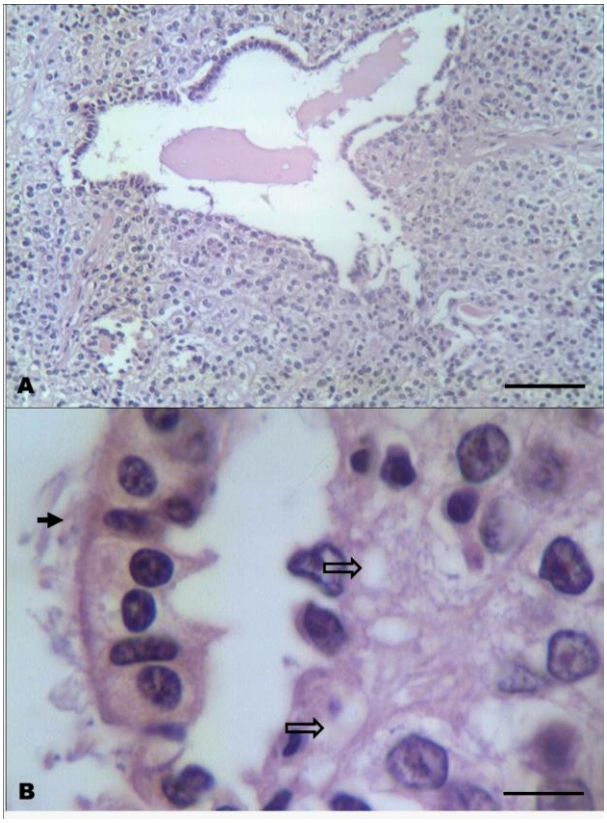

Figure 4. The large dilated structure contains an eosinophilic material and is lined by columnar ciliated epithelial cells (A). Higher magnification of the wall of a dilated structure; observe the ciliated luminal epithelia (black arrow) and adjacent clear cells that are either vacuolated (opened arrows) or containing lipid-like droplets (B). (Hematoxylin and Eosin; Bar, A 100 µm; B, 20 µm).

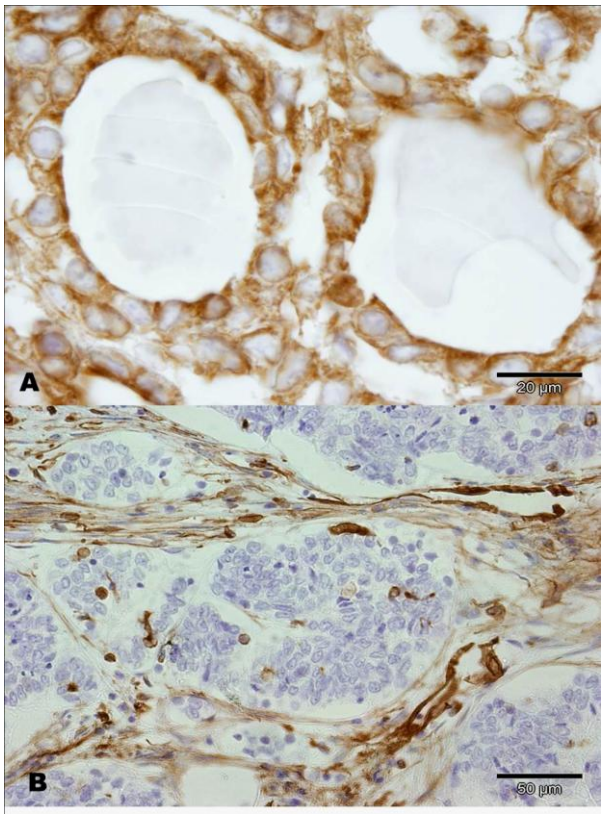

Figure 5. Immunohistochemical features of thymic adenoma in a goat. The neoplastic epithelial cells expressed positive immunoreactivity to cytokeratin (A) and reacted negatively to vimentin (B). There is positive vimentin immunoreactivity to the fibrous connective tissue around the epithelial cells (B). (Immunoperoxidase; Bar: A, 20 µm; B 50 µm).

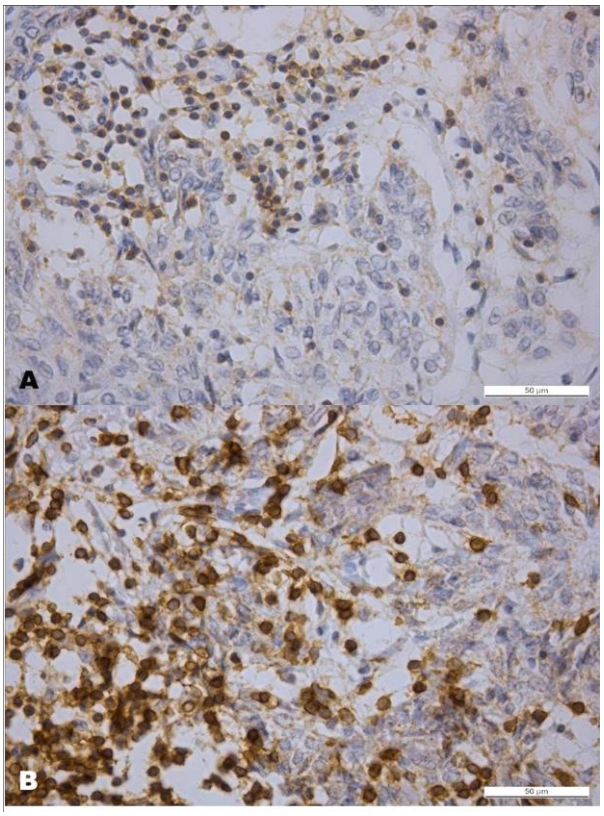

Figure 6. Lymphocytic immunoreactivity of a thymic adenoma in a goat. Cortical lymphocytes were labeled with CD 2+ (A) and their medullary counterparts expressed CD3 (B). (Immunoperoxidase; Bar: A-B, 50 µm).

Most thymomas of goats, as in this case, have occurred as benign neoplastic growths (6, 11); there is one description of dissemination to the thoracic pleura cavity, the spleen, and lung (9). Nevertheless, thymomas in domestic animals are more frequently described as benign rather than malignant neoplastic growths (7), with several descriptions of malignant thymomas occurring in the horse (5, 14, 17). The overall incidence of reported cases of thymomas in domestic animals appears to be relatively low when compared to other neoplastic diseases. In an abattoir survey done in Great Britain (13), the incidence of thymomas relatively to other tumors was 4.97% (15/302) for cattle, 0.93% (1/107) in sheep with no cases observed in swine; where the reduced number of cases was attributed to the early age at which sheep and pigs were slaughtered and it was concluded that thymomas are lesions of adult animals (13). Alternatively, histological evidence from this study suggest that these tumors might represent embryological alterations that are manifested in adult

animals, which might be incidental findings in domestic animals (7), since most commonly associated clinical manifestations are nonspecific and can be related to several disease conditions. In domestic animals, thymomas are frequently described as large, space-occupying lesions (2, 4, 9, 11), which would require a good period of time to become established before any clinical manifestation can be directly associated with the growth. In this case, the animal had a large space-occupying intrathoracic tumor which resulted in compressive atrophy to the adjacent organs; similar results have been described in cases of caprine thymoma (6, 9, 11). Although the clinical manifestations of this goat remain unclear, these large neoplastic growths in this specie have been previously related with congestive heart failure (9, 11) and respiratory embarrassment (7, 11). Hence the gross findings of hydrothorax and ascites associated with hepatic fibrosis and pulmonary edema and congestion, observed by histology, in this goat might be the manifestations of cardiac insufficiency.

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