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Diagnosis of a cystic lymphocyte-rich thymoma in a young cat

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Abstract

Thymoma is one of the thymic epithelial tumors arising from the thymic epithelial cells of a variety of animal species including cat, cattle, dog, goat, horse, and pig. The cancer cells of thymoma are always localized within thymus. Feline thymoma was usually identified in the cranial mediastinum of elder cats. In this report, we present the full diagnostic characteristics of a young cat with a cranial mediastinal mass diagnosed as a cystic type B1 thymoma. A 3-year-old male neutered domestic short-haired cat was referred for further diagnosis due to the shortness of breath and pleural accumulation. One single cystic extra-pericardial mass was seen and the boundary between the mass and the surrounding tissue was clearly demarcated in three-view thoracic radiographs. Ultrasound showed pleural effusion and intra-thoracic mass. Pleural fluid biochemistry showed high level of triglycerides and complete blood count revealed the elevated number of basophils and high level of feline serum amyloid A (fSAA). Pleural effusion sediment cytology showed a large number of round cells, mainly small lymphocytes, as well as a moderate number of neutrophils and a small number of large lymphocytes. The high level of triglycerides in pleural fluid instead of serum and high level of fSAA seem to provide informative clues to the diagnosis of thymoma and are worthy of further investigation.

Introduction

Thymoma is one of the thymic neoplasms arising from the thymic epithelial cells of a variety of animal species including cat, cattle, dog, goat, horse, and pig.[1] Feline thymoma was usually identified in cranial mediastinum of cats at the elder age. This kind of feline neoplasm is always benign and all breeds of cat can be affected by thymoma.[2]

As in all other animals, feline thymoma has no distinguishable clinical symptoms. The common clinical signs include coughing and dyspnea; vomiting and regurgitation are also seen in some cases. The thymoma can compress the lungs, causing respiratory distress or muffled heart sounds.[3] Feline thymoma may also be associated with other disorders such as myasthenia gravis, exfoliative dermatitis, para-neoplastic syndromes or metastatic disease.[4] Diagnosis of thymoma is mainly based on diagnostic imaging and histopathological examinations. Radiograph, ultrasonography and computed tomography provide different information about the location, consistency and invasiveness of the mass and pleural effusion.[3] The proliferation status of thymic epithelial cells and the sub-type of lymphocytes involved will be determined by cytological analysis. Surgery including median sternotomy or inter-costal thoracotomy is the main treatment of choice for feline thymomas.[2]

Case Description

A 3-year-old male neutered domestic short-haired cat weighing 4.80 kg was presented to the Changzhou Hongmei Animal Hospital (Changzhou, China) for further diagnosis of a cranial mediastinal mass by the referring veterinarian. Initial presenting complaints were shortness of breath and pleural accumulation. The cat had no history of medicine use. The mass was diagnosed by three-view thoracic radiographs (Fig. 1) using Weiterui X-ray machine (VDR-1500s; Shanghai Hanqing High-tech Co., Ltd. Shanghai, China). One single cystic extra-pericardial mass was seen and the boundary between the mass and the surrounding tissue was clearly demarcated. In the supine position scan, a large amount of fluid was seen in the

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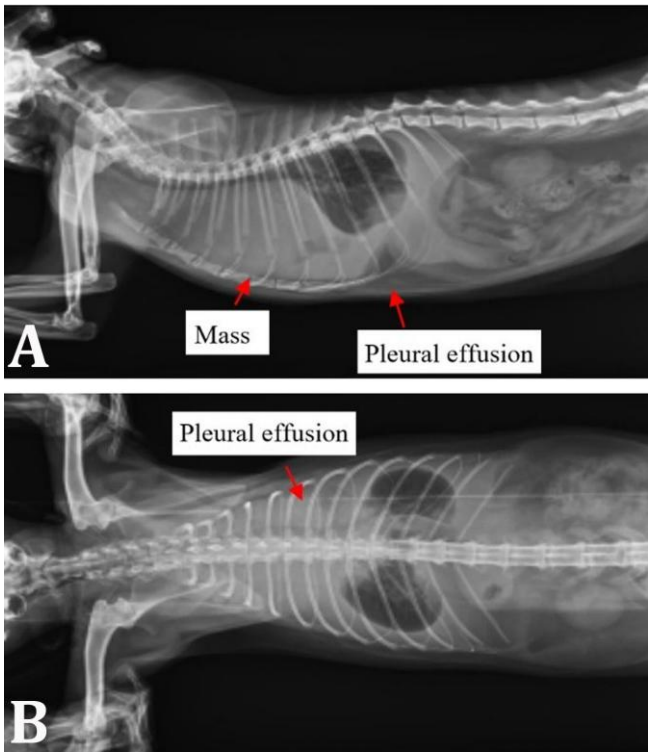

Fig. 1. A) Lateral view, and **B)** supine view of the patient. The thoracic radiographs shows a thymoma and pleural effusion in the cranial mediastinum.

thorax (Fig. 1). A low to medium-low echoic mass was seen outside the pericardium in the thorax. The thickness was about 63.00 × 48.10 mm. Ultrasound examination using MyLab™ 6 Ultrasound imaging system (Esaote, Genoa, Italy) showed pleural effusion and intra-thoracic mass (Fig. 2).

Complete blood count and biochemical analyses were performed. Pleural fluid biochemistry showed high level of triglycerides (4.24 mmol L^{-1}; Reference interval (RI): 0.11 - 1.13 mmol L^{-1}). Complete blood count revealed the elevated number of basophils (0.50 × 10^9 L^{-1}; RI: 0.01 - 0.26 × 10^9 L^{-1}). Other biochemical analyses showed the high level of serum amyloid A (SAA; 4.24 mg L^{-1}; RI: 0 - 1.99 mg L^{-1}; Table 1). The samples were taken using fine need aspiration guided by ultrasound. Cytological findings were suggestive of thymoma. Pleural effusion sediment cytology was performed by Diff Quik (DQ) staining and visualized using Leica DVM6M digital microscope (Leica Inc. Wetzlar, Germany). The results show a large number of round cells, mainly small lymphocytes, as well as a moderate number of neutrophils and a small number of large lymphocytes; but no obvious pathogenic micro-organisms were found (Fig. 3A). Combined with laboratory diagnosis, the observation was also consistent with the chylous characteristics. There was one piece of irregular, multi-lobular soft tissue from the pleural cavity. Pleural mass aspiration cytology also showed a large number of round cells, mainly small lymphocytes, and a small number of large lymphocytes; the nucleolus was obvious (Fig. 3B). In addition, eosinophils were occasionally seen and there was a neoplastic proliferation within the thymic tissue of the anastomosing islands of epithelial cells. Many cells were undergoing apoptosis and there were mild to moderate anisokaryosis and anisocytosis and admixed small lymphocytes. It had a focal cystic region appearing to be ruptured. There was also fibrous connective tissue around the mass lesion. As the same results of pleural effusion sediment cytology, no obvious pathogenic microorganisms were seen in pleural mass aspiration cytology.

Further histopathological analysis of lung sample using a digital microscope (DVM6M; Leica Inc., Wetzlar, Germany) found that the pulmonary parenchyma was diffusely and severely atelectatic, resulting in loss of most of the alveolar spaces. The alveolar walls were mildly to moderately thickened and some had smooth muscle within the alveolar septa. There was a focal cystic region and moderate granulation tissue along the pleural surface

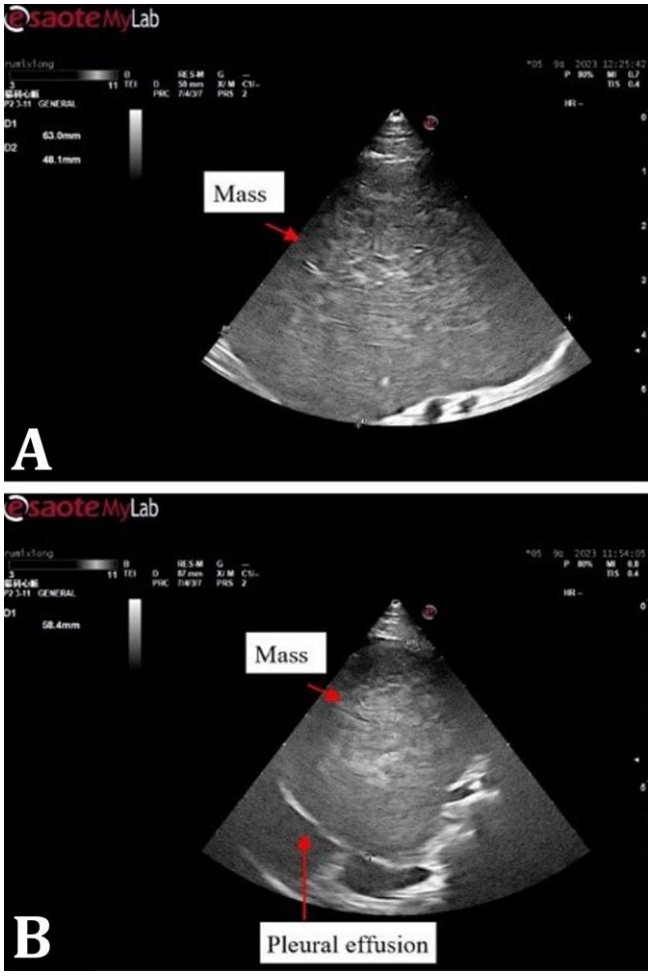

Fig. 2. Thoracic ultrasound revealed, **A)** a mild hypo-echoic mass at the right para-sternal apex with the size of 63.00 × 48.10 mm, and **B)** a large amount of pleural effusion in the thoracic cavity.

(Fig. 4A). This consisted of fibroplasia and capillaries proliferation being oriented towards the pleural surface. There were mild mesothelial cell hypertrophy and multi-focal mixed inflammation, being predominantly lympho-plasmacytic (Fig. 4B). The inflammatory foci were more prominent in the sub-pleural regions. There was marked smooth muscle hyperplasia of the arterial walls and no evidence of malignant neoplasia was found. Overall, an infectious disease was not suspected.

The thymoma mass was approached and removed through a cranial median sternotomy. The cat was initially supported in an oxygen chamber and recovered uneventfully from anesthesia.

In summary, the consensus diagnosis was that this case represents a thymoma. It had a large cystic region, which likely had ruptured resulting in the pulmonary atelectasis and pleural effusion. This also could explain the presence of chylous effusion in the patient. The thymoma had large regions of small lymphocytes, being typical for this type of neoplasm. The sub-type of thymoma, therefore, was classified as type B1. The lesions in the lungs were consisted mostly of fibrosis and sub-pleural inflammation.

Table 1. Biochemical and complete blood analyses.

Parameters	Value	Reference ranges
Pleural fluid triglycerides (mmol L^{-1})	> 4.24*	0.11 - 1.13
Complete blood count and biochemistry		
Blood glucose (mmol L^{-1})	5.94	4.11 - 8.84
Creatinine (mmol L^{-1})	86.00	71.00 - 212
Urea (mmol L^{-1})	6.40	5.70 - 12.90
Blood urea nitrogen/Creatinine ratio	18.00	-
Phosphorus ion (PHOS)	1.51	1.00 - 2.42
Calcium (mmol L^{-1})	2.38	1.95 - 2.83
Total protein (mmol L^{-1})	65.00	57.00 - 89.00
Albumin (g L^{-1})	30.00	22.00 - 40.00
Globulin (g L^{-1})	35.00	28.00 - 51.00
Albumin/globulin ratio	0.90	-
Alanine aminotransferase (U L^{-1})	20.00	12.00 - 130
Alkaline phosphatase (U L^{-1})	31.00	14.00 -111
Glutamyltransferase (U L^{-1})	0.00	0.00 - 4.00
Total bilirubin (mmol L^{-1})	< 2.00	0.00-15.00
Cholesterol (mmol L^{-1})	2.14	1.68 - 5.81
Triglycerides (mmol L^{-1})	0.77	0.11 - 1.13
Red blood cells ($\times 10^{12}$ L^{-1})	8.86	6.54 - 12.20
Hematocrit (%)	39.70	30.30 - 52.30
Hemoglobin (g dL^{-1})	12.60	9.80 - 16.20
Mean red blood cell volume (fL)	44.80	35.90 - 53.10
Average red blood cell hemoglobin content (pg)	14.20	11.80 -17.30
Average red blood cell hemoglobin concentration (g dL^{-1})	31.70	28.10 -35.80
Coefficient of variation in red blood cell distribution width (%)	25.70	15.00 - 27.00
Reticulocytes (%)	0.10	
Reticulocytes ($\times 10^{3}$ μL^{-1})	5.30	3.00 - 50.00
Reticulocyte hemoglobin content (pg)	16.90	13.20 - 20.80
White blood cells ($\times 10^{9}$ μL^{-1})	8.58	2.87-17.02
Neutrophils (%)	51.50	-
Lymphocyte (%)	36.60	-
Monocytes (%)	36.60	-
Eosinophil (%)	3.30	-
Basophil (%)	5.80	-
Neutrophils ($\times 10^{9}$ L^{-1})	4.42	2.30 - 10.29
Lymphocytes ($\times 10^{9}$ L^{-1})	3.14	0.92 - 6.88
Monocytes ($\times 10^{9}$ L^{-1})	0.24	0.05 - 0.67
Eosinophils ($\times 10^{9}$ L^{-1})	0.28	0.17 - 1.57
Basophils ($\times 10^{9}$ L^{-1})	0.50*	0.01 - 0.26
Platelets ($\times 10^{3}$ μL^{-1})	439	151 - 600
Average platelet volume (fL)	15.40	11.40 - 21.60
Platelet volume (%)	0.68	0.17 - 0.86
Feline serum amyloid A (fSAA)	4.24*	0.00 -1.99
Feline pro-B-type natriuretic peptide (FBNP)	Negative	-
Cardiac troponin	0.30	0.00 - 0.90

* indicates higher value than normal range.

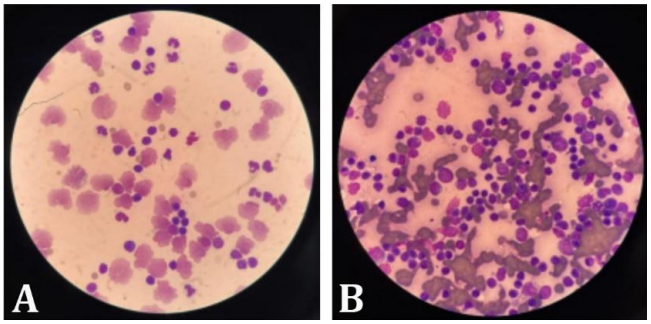

Fig. 3. Cytological smear analysis. **A)** pleural fluid, and **B)** thoracic mass. Large numbers of round cells were found in pleural fluid sediment cytology, mainly small lymphocytes, as well as moderate numbers of neutrophils and small numbers of large lymphocytes. Thoracic mass aspiration cytology shows a large number of round cells, mainly small lymphocytes, and a small number of large lymphocytes having obvious nucleoli. In addition, eosinophils were occasionally seen, and no obvious pathogenic micro-organisms were found (Diff Quik staining, 100×).

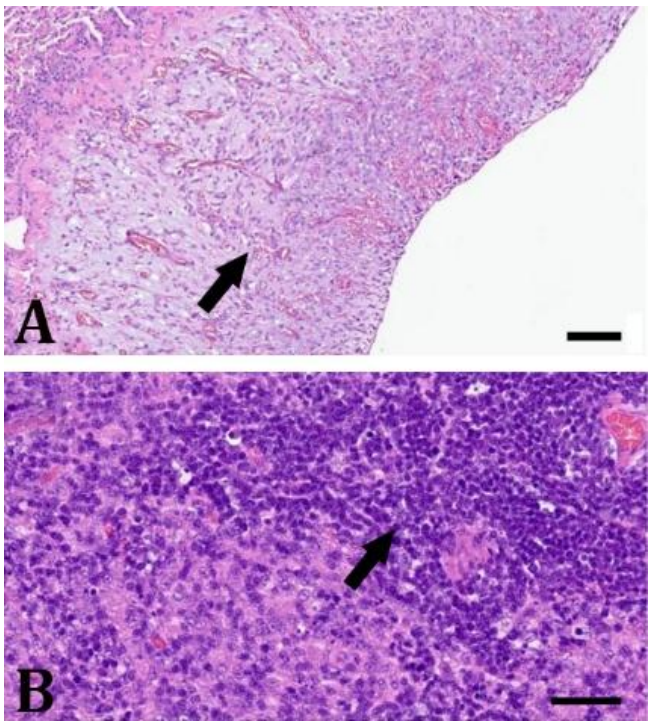

Fig. 4. Histopathological analysis. **A)** Pleural granulation tissue (arrow) in the lung sample, and **B)** lympho-plasmacytic cells (arrow) in the thymic mass, (Hematoxylin and Eosin staining, bars = 100 µm).

Discussion

Both thymoma and thymic carcinoma are thymic epithelial tumors being generated from the outer layer of thymus. The cancer cells of thymic carcinoma grow fast, look more abnormal, and are more likely to metastasize into other parts of the body. In contrast, tumor cells of thymoma are always localized within thymus, grow slowly, and look normal. According to the classification system developed by the World Health Organization, thymoma is classified into types A, AB, B and C. Type B is further divided into B1, B2, and B3.[5] Type A thymoma is composed of usually bland spindle or oval tumor cells with few or no admixed immature lymphocytes in the tumor.[5] Type AB thymoma is made up of cells like type A; but, there are large numbers of lymphocytes (it is also called mixed thymoma).[5] Type B-1 thymoma is composed of normal cells with lots of lymphocytes. It is also called lymphocyte-rich thymoma, predominantly cortical thymoma or organoid thymoma.[5] Type B-1 displays the cyto-architectural features of the non-involuted normal thymic cortex, accompanied by regions of medullary differentiation. Type B-2 thymoma is a lymphocyte-rich thymic epithelial tumor composed of enlarged polygonal tumor cells being accompanied by numerous immature lymphocytes and is often associated with myasthenia gravis. The tumor cells occur at a density higher than that of the normal thymus and of type B-1 thymoma. Type B-3 thymoma is predominantly composed of mildly or moderately atypical polygonal tumor cells, accompanied by small numbers of non-neoplastic immature lymphocyte.[5] Type C is actually the thymic carcinoma made up of very abnormal thymic epithelial cells and has a poor prognosis compared to thymoma.[5] The case reported here is consistent with type B1 in that mass has mostly normal-looking thymus cells; but, it contains a large number of small lymphocytes.

The thymoma patient in this study had high level (> 4.24 mmol L^{-1}) of triglycerides in pleural fluid, but had normal level of those (0.77 mmol L^{-1}) in the serum, representing a phenomenon being worthy of further investigation. Triglycerides are important fats providing energy and their level can serve as an indicator for the disease development. For example, study of 185 human sub-clinical atherosclerosis patients with primary hypertension showed that triglyceride-glucose (TyG) index values were positively associated with target organ damage (TOD), not merely sub-clinical atherosclerosis, indicating that the level of triglyceride is an important factor in predicting the presence of TOD.[6] A total of 382 operated patients were also studied to determine the direct relationship between thyroid papillary cancer and TyG index.[7] It was found that TyG index was statistically higher in the thyroid papillary cancer group compared to the non-malignant patients. The results demonstrated the predictive role of TyG index in differentiating thyroid papillary cancer from non-malignant thyroid lesions, which can be used to identify people at high risk of thyroid papillary cancer for better formulation of treatment.

Serum amyloid A as an acute phase reactant is an inflammatory marker in inflammation and other diseases of both human beings[8] and cats.[9] The concentration of feline SAA(fSAA) can increase rapidly to significantly high

levels in response to injury, renal failure, or infectious diseases.[10] Cats with metabolic or endocrine diseases also show high SAA concentration.[11] The thymoma patient in our study had a high level of fSAA, indicating the potential association. In human patients, SAA concentration was considered to be a risk factor of diabetes and metabolic syndrome and may be related to the development of cardiovascular disorders and nephropathy.[12] The SAA concentration could function as a prognostic marker in human patients with rheumatoid arthritis.[13] In human medicine, SAA is not only a marker of existing inflammation, but also a prognostic marker for several diseases including inflammatory diseases, neoplasia, and also non-inflammatory diseases such as diabetes.[14] The fSAA was evaluated as a prognostic marker in cats with various diseases.[15] In cats, SAA concentration was reported to be increased also in neoplastic and non-inflammatory diseases.[11] The role of fSSA as a prognostic marker in TETs needs further investigation.

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Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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