ESVCP Mystery Case 2020

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SPECIMEN: BAL right caudal lung lobe, cytocentrifuge preparation, Modified Wright stain

SIGNALMENT: Feline, 4-year-old, male, castrated Maine Coon, 7 kg

HISTORY AND CLINICAL FINDINGS: The patient was presented to the Purdue University Veterinary Teaching Hospital (PUVTH) for evaluation of a one-year history of a chronic dry cough, with worsening of a radiographic bronchial pattern in the last two months. He had a previous diagnosis of feline asthma, whose treatment was oral prednisone and fluticasone inhaler; both were still being administered daily to the cat. On physical examination, the cat had a mild fever (39.8 °C), increased respiratory rate (48 bpm), and increased lung sounds bilaterally. Thoracic radiographs confirmed the bronchointerstitial lung pattern and also found numerous variable sizes ill-defined, opaque, soft tissue nodules throughout the pulmonary parenchyma. One patchy mass effect was also noted in the right caudal lung lobe. His CBC and urinalysis were unremarkable. His chemistry panel (Vitros 5,1 FS Chemistry System, Ortho-Clinical Diagnostics, Raritan, NJ, USA) revealed only a moderate hyperproteinemia (8.3 g/dL, reference interval [RI] 5.5-7.1 g/dL) and hyperglobulinemia (4.8 g/dL, RI 2.3-3.8 g/dL). Bronchoalveolar lavages of the right caudal and two left caudal lung lobes were performed.

CYTOLOGICAL IMAGES:

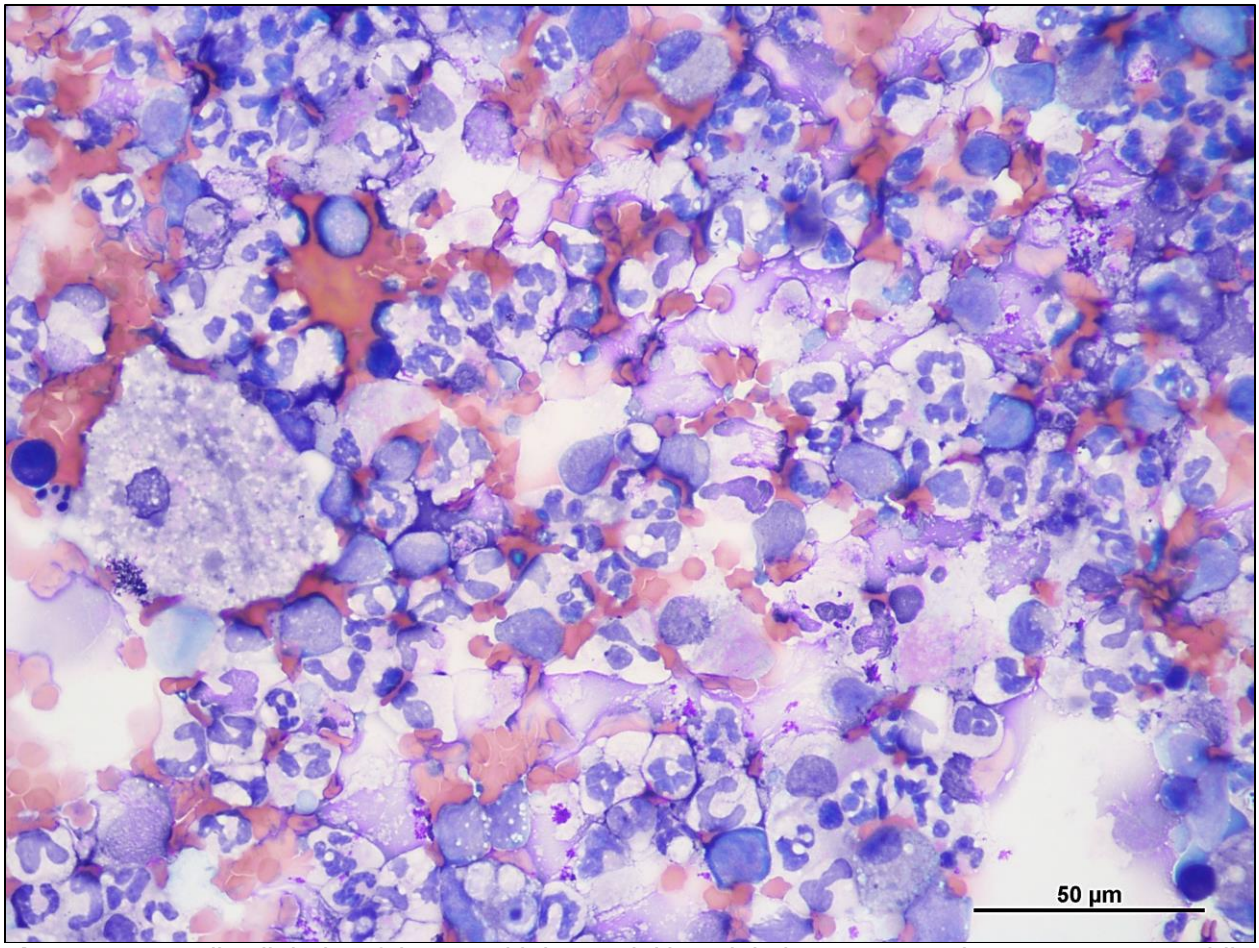

Figure 1: Overall cellularity of the BAL (right caudal lung lobe). Numerous degenerate neutrophils are present, in addition to lymphocytes, activated macrophages, and plasma cells in a background with moderate numbers of red blood cells and numerous nonintact cells. Modified Wright stain (50x objective).

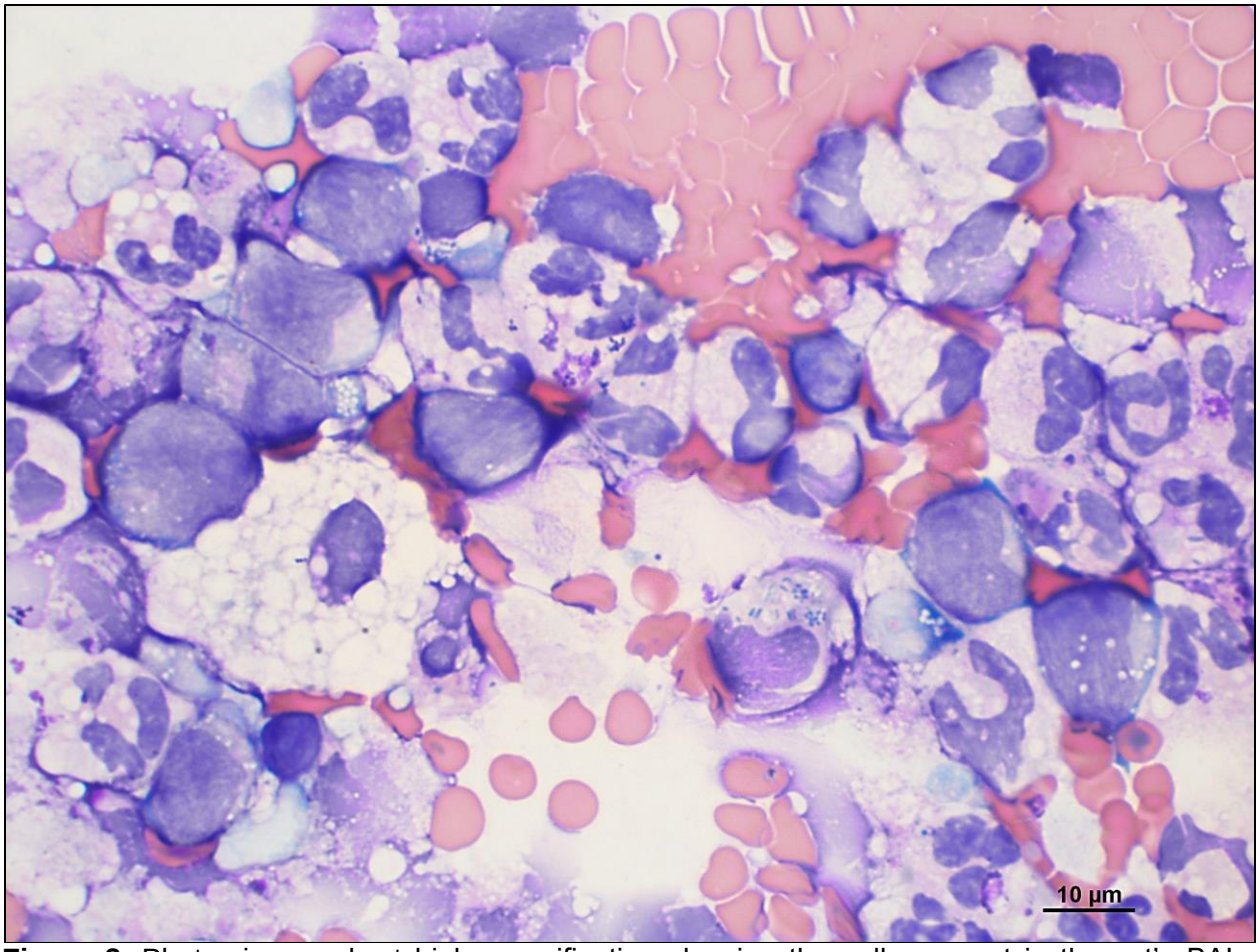

Figure 2: Photomicrograph at high magnification showing the cells present in the cat's BAL. Modified Wright stain (100x objective).

QUESTIONS:

1. What are the possible differential diagnoses for the pulmonary mass based on the BAL findings? (Mark all pertinent options).
   - ☐ Granulomatous disease
   - ☑ Severe persistent asthma with secondary infectious pneumonia
   - ☐ Epithelial neoplasia
   - ☑ Round cell neoplasia
   - ☐ Mesenchymal neoplasia

CYTOLOGIC DESCRIPTION: The specimen is highly cellular. The cytocentrifuge preparation has densely distributed inflammatory cells in a background with moderate numbers of red blood cells. It consists of >90% degenerate neutrophils and <10% macrophages and lymphocytes. Low numbers of plasma cells and rare hemosiderin-laden macrophages are also present. Neutrophils often contain phagocytized bacteria rods and coccobacilli. Extracellular long rods are also identified. Lymphocytes range from a few small, well-differentiated cells to moderate numbers of intermediate to large cells. The latter occasionally contain immature chromatin and one prominent, round to irregularly shaped nucleoli; occasional macronucleoli are seen. A few

squamous epithelial cells and Simonsiella sp. are observed, representing oropharyngeal contamination.

CYTOLOGIC INTERPRETATION: Septic suppurative inflammation with the presence of bacteria coccobacilli and rods; evidence of mild chronic hemorrhage.

ADDITIONAL FINDINGS: Samples from the tracheal wash (TW) and all additional BALs revealed similar findings: septic suppurative inflammation as well as the presence of a few intermediate to large lymphocytes.The BAL bacterial culture was positive for *Streptococcus felis* and *Pasteurela multocida*. A broncoscopic cup biopsy of a mass located within the bronchial lumen of the right lung was obtained for histopathologic evaluation along with impression smears of the biopsy for cytologic evaluation. On cytology, the specimen consists of a monomorphic population of intermediate to large lymphocytes in a moderately hemodiluted background. The monomorphic population had a small amount of blue to dark blue cytoplasm that occasionally contained pinpoint colorless vacuoles. The nuclei were round, eccentrically placed, and exhibited a fine chromatin pattern. One to two round to irregular-shaped prominent nucleoli were seen. Small lymphocytes and plasma cells were also present (approximately 40% of the lymphoid population). Nondegenerate neutrophils were present in numbers and proportions compatible with the amount of blood. Activate macrophages were observed in low numbers. No infectious agents were identified (**Figure 3**). On histology, the diagnosis was inconclusive, given the small sample size with crushing artifact. The sample was partially lined by hypertrophic mesothelium or respiratory epithelium. It contained numerous round cells displaying anisocytosis and round nuclei. The lung mass aspirate and one cytocentrifuge preparation of right and left caudal lung lobes each were submitted to PCR antigen receptor rearrangement (PARR, Clinical Immunology Laboratory of Colorado State University). The results indicated a clonally rearranged immunoglobulin gene in all samples. For confirmation, CD3 (T cell markers) and Pax5 (B cell marker) immunohistochemistry staining was also performed in the mass. The neoplastic cells were strongly positive Pax5. Additionally, the cat was negative for FIV, FeLV, heartworm antigen and antibody, and Blastomyces urine antigen. Given the lack of clinical, radiologic, and ultrasonographic evidence of any other lesion in the body, the final diagnosis of primary pulmonary lymphoma was made.

DIAGNOSIS: Primary pulmonary B cell lymphoma with secondary bacterial pneumonia

CLINICAL OUTCOME/FOLLOW-UP: The patient received one dose of L-asparaginase and was treated for his bacterial pneumonia while in the hospital. He was discharged six days later with clinical and radiological improvement of his lung diseases. He returned to PUVTH for CHOP chemotherapy protocol. On his last visit four months after initial diagnosis, the cat showed significant improvement of his pulmonary lymphoma (**Figure 4**).

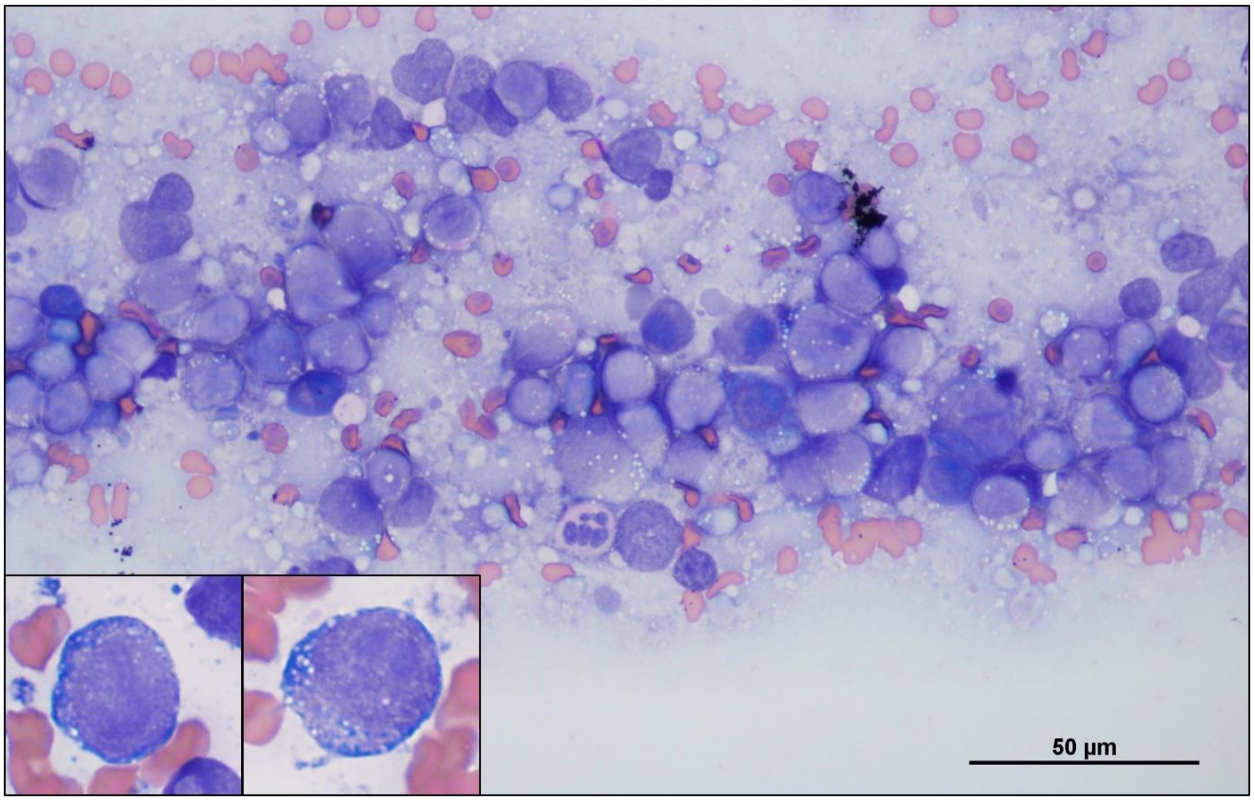

Figure 3: Photomicrograph of the impression smear cytology showing numerous intermediate to large lymphocytes (10-25 µm). Modified Wright stain (50x objective). In the inlet, two lymphocytes in high magnification. Modified Wright stain (100x objective).

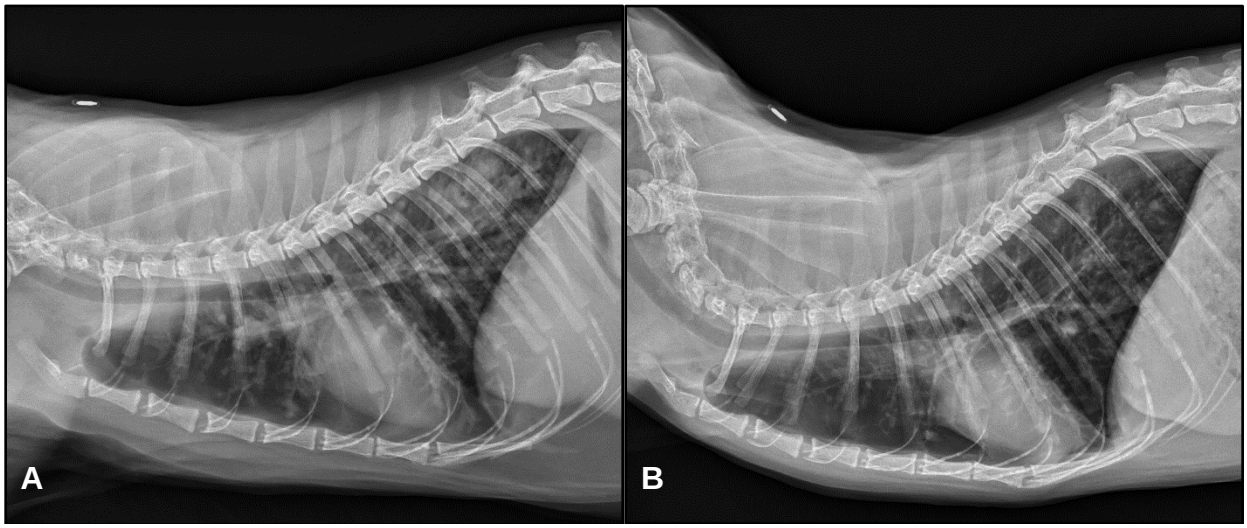

Figure 4: Right lateral thoracic views on digital radiographs. **(A)** Mixed, predominantly bronchointerstitial pattern and structured nodular pattern on presentation (January 6th, 2020) can be observed. **(B)** The last imaging findings four months after initial presentation, showing a reduction in the diffuse soft tissue throughout the lung lobes.

DISCUSSION:

Lymphoma is the most common hematopoietic neoplasia affecting dogs and cats. Extranodal lymphomas can affect different tissues, with the gastrointestinal tract as the most

prevalent location.[1] Primary pulmonary lymphoma is rare in humans, accounting for less than 1% of the cases.[2] In cats, there is limited literature related to the prevalence of feline primary pulmonary lymphoma. Following the classification of lymphomas proposed by Gabor et al.[3], lymphomas could be anatomically divided into nodal, abdominal, mediastinal, atypical, and mixed. Pulmonary lymphoma would fall into the atypical presentation. One study showed a prevalence of 21% of atypical lymphomas. Among the latter, only 1% was located in lower respiratory system.[4] Approximately 13% of lymphomas occurring in other organs metastasize to the lungs.[2]

The radiographic appearance of pulmonary lymphoma is highly variable, ranging from no radiological abnormalities to unstructured interstitial pattern to alveolar disease and pulmonary masses. However, pulmonary masses and/or nodules and bronchial infiltrate are the most common findings. In our case, the concurrent bacterial pneumonia and feline asthma were confounding factors in the radiographic evaluation.[5]

Although intermediate to large lymphocytes displaying nuclear criteria of malignancy were present in the luminal respiratory samples (TW and BALs), the presence of marked septic suppurative inflammation obscured the presence of lymphoma. There are no reports of how frequently lymphoma cells present in the lower respiratory tract would exfoliate into the lumen. Additionally, cytopathology correlates with histopathology findings in 82% of the cases.[6]

The sensitivity to detect B cell and T cell lymphoma in cats is 87 and 97%, respectively, while the specificity is 100% in both types. The lower sensitivity for B cell lymphoma diagnosis can be explained by the high degree of somatic hypermutation found in B cell lymphomas, which would interfere in the primer annealing.[7] In our case, the two BALs submitted for PARR had a low amount of DNA, which could lead to false-positive results. However, these samples produced an amplicon identical to the one from the pulmonary mass (per report provided).

The present case of primary pulmonary lymphoma has presented a good response to the chemotherapy protocol implemented. Although lymphomas exhibit variable clinical presentations, the median survival time is 536 days, regardless of therapy modality.[8] The challenge between matching radiologic, cytologic, and histologic diagnosis lies in the limitations of each technique. The cytologic evaluation of a BAL represents the collection of findings from a whole lung lobe, while the tissue biopsy is limited to a target region. The thoracic radiography is essential to establish the localization of a given lesion; however, whether the increased radiographic density is the result of cellular infiltration, edema or fibrosis cannot be determined solely with this technique.[9] In this case, the cat had more than one lung disease, the tissue biopsy had low diagnostic quality, and the inflammation obscured the presence of only a few cells displaying criteria of malignancy. The use of PARR was fundamental for the final diagnosis in this lymphoma case.

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