WHAT IS YOUR DIAGNOSIS?

A six-year and eight-month old, male entire cross breed was presented to the R(D)SVS Cardiopulmonary service for investigation of a 2-week history of tachypnoea. A mediastinal mass was suspected on the thoracic radiographs performed by the referring veterinarian. At presentation, the respiratory rate was 24 breaths per minute, the breathing pattern was normal and auscultation of the lung fields was unremarkable. However, heart sounds were muffled on the left side, and thoracic percussion was dull in the left cranial lung field.

1) What are your differential diagnoses for a mediastinal mass?

2) How would you evaluate this case further?

3) How would you treat and monitor this dog?

1. Differential diagnosis for a mediastinal mass
   - Non-neoplastic mediastinal masses
     o Cyst (pleural, branchial, lymphatic, bronchogenic or thymic origin)
     o Haematoma
     o Pyogranuloma
     o Abscess
     o Lymphadenopathy
   - Neoplastic mediastinal masses
     o Lymphoma
     o Thymoma
     o Histiocytic sarcoma
     o Chemodectoma
     o Ectopic thyroid carcinoma
     o Others...
2. **Further evaluation**

Haematology and serum biochemistry were unremarkable. A thoracic CT scan confirmed a large poorly contrast enhancing mass in the cranial mediastinum, with a propensity towards the left (Figure 1). The mass could also be visualised on ultrasound, and appeared as large, hypoechoic, relatively homogeneous, moderately vascular and occupying the full width of the cranial thorax (Figure 2).

An ultrasound-guided fine-needle aspirate of the mediastinal mass was obtained. On cytology, a population of large lymphoid cells predominated. The nuclei were rounded and occasionally indented, the chromatin pattern was with multiple small to large nucleoli. The cytoplasm was dark blue, often with a clear perinuclear zone, and occasionally containing small vacuoles. Occasional mitotic figures were present. (Figure 3). These features were consistent with a **large cell lymphoma**.

Following the diagnosis of lymphoma, staging was completed with an abdominal ultrasound. A 2 cm hypoechoic mass with mildly indistinct margination was noted within the spleen. Two para-aortic lymph nodes were enlarged (1.1cm), rounded and hypoechoic. Cytology of the splenic mass confirmed extension of the mediastinal lymphoma.

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**Figure 1:** Thoracic CT scan showing a large mass within the left mediastinum

**Figure 2:** Thoracic ultrasound showing a large mass within the cranial mediastinum
3. Treatment and monitoring

A 19-week CHOP protocol was initiated. Complete remission was confirmed on thoracic radiographs at the end of the first cycle. Thoracic radiographs were repeated at the end of his chemotherapy protocol. A possible early relapse was suspected, but since his response status was unclear, he received his final doxorubicin as planned. Thoracic radiographs were repeated a month later, and unfortunately confirmed a relapse of his lymphoma (Figure 4), although the dog remained asymptomatic.

![Figure 3: Cytology of the mediastinal mass, consistent with a large cell lymphoma.]

![Figure 4: Dorso-ventral and right lateral thoracic radiographs a month after completed a 19-week CHOP. Relapse was confirmed.]

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A lomustine/prednisolone rescue protocol was initiated. Thoracic radiographs were repeated after two doses of chemotherapy, and were consistent with a complete clinical response. After having received three doses of lomustine, he developed a grade 3 ALT toxicity (602 IU/L, RI 30-120). His chemotherapy was delayed and a course of S-adenosine methionine (SAMe) / silymarin was prescribed. A week later, his ALT toxicity had not improved. His fourth dose of lomustine was administered with a 10% dose reduction, and his hepatoprotective supplements were continued. Three weeks later, his ALT toxicity continued to progress (1684 IU/L, RI 30-120). Thoracic radiographs were consistent with ongoing complete clinical response, and his chemotherapy treatment was stopped. A month later, his ALT was markedly decreased (216 IU/L, RI 30-120) and was within reference interval a few months later. His hepatoprotective supplements were stopped. The dog continued to be rechecked with monthly physical examination for the following 18 months. Thoracic radiographs were performed monthly initially and bimonthly after a few months due to financial constraints. The rechecks were spaced to every 2 months afterwards. Two years after initial diagnosis, the dog is still doing well and in complete clinical remission.

Discussion

The agreement between cytological and histological classification of mediastinal masses in dogs has been reported as almost perfect. This is particularly true for the two most common differentials, lymphoma and thymoma. Most of primary canine mediastinal lymphomas are high grade T-cell lymphomas, often with a lymphoblastic or large cell morphology. Sonographic characteristics of thymomas and mediastinal lymphomas has been reported, and thymomas are more commonly heterogeneous and cystic compared to lymphomas. Contrast-enhanced ultrasonography of mediastinal masses has also been described, but its role as a diagnostic tool remains unknown. If a definitive diagnosis cannot be achieved based on cytology, other techniques such as flow cytometry, PARR analysis or true-cut biopsies can be considered.

CHOP-based chemotherapy protocols appeared to be associated with an improved survival, and are currently the treatment of choice for canine primary mediastinal lymphomas. If this treatment fails, a rescue chemotherapy protocol could be attempted. Radiation therapy has also been used anecdotally as consolidation or rescue, but further investigation is needed to better understand its potential benefit for the management of this cancer.

One of the unique toxicities of lomustine in dogs is hepatotoxicity. The mechanism of hepatic injury is poorly understood, and it has been suggested that its hepatotoxicity might be related to cumulative dose although it remains difficult to predict. In the majority of cases, dogs remain asymptomatic and the hepatic injury resolves. The concurrent use of hepatoprotective supplements (SAMe, silybin) in dogs receiving lomustine has been advocated, since it can minimise the increased liver enzyme activity. However, these supplements are associated with an increase in hepatic glutathione concentration, and could theoretically affect the metabolism of chemotherapeutic drugs. Furthermore, SAMe can interact directly with cancer cells and affect chemotherapy efficacy. Further investigation is needed to determine the interaction of these supplements with chemotherapeutic drugs in vivo.
References


