EXTENDED ABSTRACT

A case of primary papillary disseminated adenocarcinoma of canine lung

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Abstract Primary lung tumors are rare in dogs, whereas pulmonary metastatic neoplastic involvement is common. We describe a case of a 12-year-old male, mixed-breed dog with a 3-month history of coughing and dyspnea. The investigating protocol, which also includes transcutaneous pulmonary biopsy, allowed a diagnosis of lung adenocarcinoma that necroscopic findings confirmed as a primary neoplasia. The tumor exhibited a nodular-disseminated growth, mimicking the metastatic involvement of the lung, instead of the single-mass appearance that has been observed by other authors. The present report indicates that, although the incidence of canine primary lung neoplasms is markedly low, this condition must be considered in the differential diagnosis of lung diseases that cause coughing and dyspnea in older dogs.

Keywords Dog · Lung tumors · Adenocarcinoma · Diagnosis

Abbreviations
BAL   Broncho-alveolar lavage
AlP   alkaline phosphatase
ALT   alanine transferase
γ-GT   γ-glutamyltransferase

Introduction

In dogs, primary lung tumors are rare (1.2%) (Ogilvie et al. 1989; Sato et al. 2005), whereas metastatic involvement of this organ occurs frequently (Castellano et al. 2006). As reported in the literature (Jennier and Sorenmo 2004; Marconato 2005), primary tumors are more

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often described in geriatric dogs (9.3–10.9 years), especially in boxers, labrador retrievers, springer spaniels, golden retrievers, and Irish Setters. The latter tumors normally appear as a single mass in the right diaphragmatic lobe, as this region is larger on the right than on the left (Jennier and Sorenmo 2004). Specifically, adenocarcinoma is usually located in peripheral lung tissue and rarely disseminates into multiple small nodules (Jennier and Sorenmo 2004; Marconato 2005; Moulton 1990). For these reasons, we describe a case of primary papillary adenocarcinoma of the lung, which was characterized by disseminated development, emphasizing the necessity to take into consideration this neoplasia in the differential diagnosis of patients with clinical signs of chronic pulmonary pathology even when single masses are absent upon thoracic radiographic examination.

Materials and methods

This study was conducted on a 12-year-old, male, mixed-breed dog that weighed 22 kg, and was referred to the Veterinary Teaching Hospital of the University of Perugia due to a 3-month history of coughing and dyspnoea. Moreover the subject partially, but only transiently, recovered when antibiotics and corticosteroids were administered. The dog was physically examined, and additional testing was performed, including venous blood draws for hemocytometric analysis and a complete biochemistry profile; arterial blood draw for the measurement of blood gases; thoracic X-rays; bronchoscopy associated with broncho-alveolar lavage (BAL) and biopsy of the bronchial mucosa; thoracic ultrasound, and lung transcutaneous biopsy accordingly to Griffin's protocol (Griffin 2004). BAL was used to perform bacteriological, mycological, and cytological evaluations, whereas biopsy samples underwent histopathological examination. Furthermore, we correlated the data with those of anatomohistopathology.

Results

Upon clinical examination, the animal appeared depressed and presented tachypnea (40/min), both inspiratory and expiratory distress, and a heart rate of 110 beats per min. A dry cough was easily induced by palpation/traction of the trachea, presenting a strong vesicular lung murmur that spread bilaterally. Blood analyses showed an increased alkaline phosphatase (AlP), alanine transferase (ALT), and γ-glutamyltransferase (γ-GT) activities of 275 U/L, 45 U/L, and 14 U/L, respectively. Blood gas analysis confirmed the presence of acidosis from total respiratory failure (pH 7.32, pO_2 62 mm Hg, pCO_2 58 mm Hg, and HCO_3^- 16 mEq/L). Latero-lateral and dorso-ventral X-rays of the thorax showed a nodular-interstitial and bronchial pattern that involved both lungs (Fig. 1). The performed bronchoscopy showed evidence of a chronic exudative broncopathy, as well as the presence of disseminated miliariform nodules on the mucosal surface (Fig. 2). Bacteriological and mycological exams were both negative, and cytological specimens were compatible with chronic inflammation, containing numerous macrophages at various stages of activation. Histological evaluation of pulmonary biopsy samples allowed a diagnosis of adenocarcinoma, but did not distinguish its origin as either primary or metastatic. A gross anatomopathological examination showed an increase in the volumes of both lungs; whitish nodules of 1–3 mm in diameter that were disseminated into the parenchyma and confluent, appearing as a spread netlike texture in section (Fig. 3); an increase in tracheo-bronchial lymph node volume; and hepatomegaly with an increase in lobular texture. Histopathological specimens

Fig. 1 Latero-lateral view. Nodular-interstitial and bronchial pattern is shown

revealed the formation of tubules and papillae delineated by cubic cells with a basal nucleus; evidence of 1–2 nucleoli and scarce apical basophilic cytoplasm, growing in a multifocal manner and of infiltrating nature not delimited; a marked anisokaryosis and anisocytosis; an elevated mitotic index (15–20/10 hpf); intra-alveolar and intravascular multifocal emboli, more frequently found in peribronchial lymphatic vessels and lymph nodes, and widely infiltrated by neoplastic tissue; and hepatic centrolobular diffuse degeneration, due to a state of hypoxemia. Immunohistochemistry with anti-thyroid transcription factor-1 antibodies, positive in disseminated cells, allowed the classification of this neoplasia as primitive pulmonary papillary adenocarcinoma (Bettini et al. 2009).

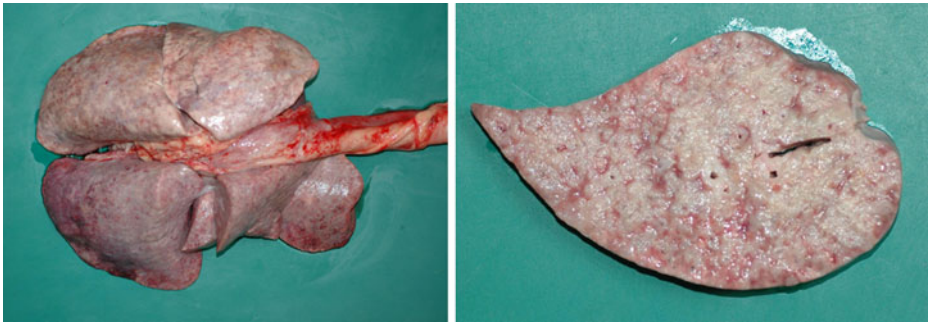**Fig. 2** Disseminated nodular lesions on the mucosal surface

Fig. 3 Gross lung appearance (left) and lung section (right). Note the diffuse texture

Discussion

The case of a primary disseminated papillary adenocarcinoma, rarely described in the literature (Jennier and Sorenmo 2004; Marconato 2005), led us to a critical review of its adopted diagnostic protocol. The clinical signs were similar to those normally observed in chronic bronchopneumopathies in dogs. With regard to the laboratory analysis results, the increases in serum levels of AlP, γ-GT, and ALT are most likely related, in our opinion, to liver damage, also evident in histopathology specimens, and secondary to chronic hypoxemia. The latter condition is in agreement with the arterial blood gas values, suggesting that the structural damage was in such an advanced stage that it causes total respiratory failure even at rest. Among the instrumental investigations performed, ultrasonography provided limited information because the most superficial layers of the lungs were under continuous ventilation, preventing the penetration of ultrasound. Chest X-rays instead allowed for a more focused diagnosis, because the images were compatible with metastatic lung cancer, pulmonary mycosis, and those conditions characterized by interstitial-nodular patterns (Burk and Feeney 2003). However, such images did not provide sufficient guidance on the nature of the neoplasia because the disseminated nodular appearance was not consistent with the finding of a single mass, which is a characteristic of primary adenocarcinoma (Jennier and Sorenmo 2004; Marconato 2005). Moreover, even though bronchoscopy and BAL did not allow the identification of the neoplasm, they helped rule out infection. The finding of tumor cells in BAL aliquots is in fact quite rare, and the absence of the latter should not be considered discriminatory because lavage involves the bronchial tree and mucus will sometimes prevent the lavage fluid from reaching the bronchioles (Cowell et al. 1989). Additionally, the visualization of tumor cells in cytological specimens can be challenging because of the concomitant presence of inflammatory cells that have a greater tendency to exfoliate and are therefore found in higher concentrations in the retrieved fluid (Cowell et al. 1989; Jennier and Sorenmo 2004).

We would like to share some thoughts on transcutaneous biopsy sample procedures as it turned out to be the only investigation that allowed us to make a clear diagnosis, even without the recognition of primary lung disease. In our experience, the above-mentioned technique should be used more frequently in the diagnoses of diseases that involve the pulmonary parenchyma, even if the procedure can lead to severe complications, such as a pneumothorax or hemothorax. While such incidents did not occur here, it is true that lung biopsy guidance is often precluded in all cases where lung ultrasound is difficult. In light of these discussions, the pathology described, although rare, should always be included in a differential diagnosis of geriatric patients with chronic cough and dyspnoea. Additionally,

the radiographic findings of an interstitial-nodular pattern should not preclude the possibility of primary adenocarcinoma.

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