Idiopathic Pulmonary Fibrosis in West Highland White Terriers

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KEYWORDS

• Dog • Interstitial lung disease • Bronchoalveolar lavage • Arterial blood gases
• HRCT • Biomarker

KEY POINTS

- Canine idiopathic pulmonary fibrosis (CIPF) is a chronic, progressive, interstitial lung disease of unknown cause affecting mainly middle-aged and old West Highland white terriers.
- Typical findings are cough, exercise intolerance, Velcro crackles, an abdominal breathing pattern, and hypoxemia.
- Bronchial changes are present in many dogs and bronchoalveolar lavage fluid analysis usually shows an increased total cell count.
- Diagnosis is one of exclusion and often requires either high-resolution CT imaging or histopathology of the lung tissue, which is seldom performed on living dogs.
- CIPF shares several clinical findings with human idiopathic pulmonary fibrosis (IPF); however, in histopathology, CIPF has features of human IPF but also of human nonspecific interstitial pneumonia.
- No effective treatment exists, but corticosteroids and theophylline can ease clinical signs in dogs. Pirfenidone is the only licensed drug to treat IPF in humans, but it does not result in cure.

INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive interstitial lung disease (ILD) of unknown cause.[1] The disease is recognized in humans,[1,2] cats,[3,4] and dogs.[5–8] The prevalence and incidence of canine IPF (CIPF) are currently unknown and can be difficult to estimate. Recognizing a dog with early CIPF is challenging

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because the slowly progressive clinical signs can be confused with aging. Additionally, confirming CIPF requires very thorough examinations.

The first case series of CIPF in West Highland white terriers (WHWTs) was published in the late 1990s.[5] Reports of CIPF in other dog breeds (Staffordshire bull terrier, Schipperke, and Bull terrier) were described around the same time.[6,9] More recent studies of CIPF have aimed at defining the clinicopathologic findings of diseased WHWTs compared with controls matched by age and breed,[8] revealing histopathologic features,[7,10] findings detected on high-resolution CT (HRCT),[11] and assessing pulmonary hypertension (PHT) with Doppler.[12] Other studies include an investigation of surfactant protein (SP) C,[13] different potential fibrosis biomarkers,[14,15] and proteomic analysis of bronchoalveolar lavage (BAL) fluid (BALF) of WHWTs with CIPF.[16] Many questions regarding the disease remain unanswered. Cause and pathogenesis of the disease and the role of genetics are poorly understood and, therefore, are under active research.

DEFINITION AND HISTOPATHOLOGIC FEATURES

IPF belongs to a heterogenous group of ILDs that consist of several noninfectious and nonmalignant pulmonary diseases with overlapping clinicopathologic and radiographic features. ILDs affect the pulmonary interstitium, which is the space between the capillary endothelial and alveolar epithelial basement membranes.[17] In humans, more than 200 ILDs are recognized,[17] whereas far fewer ILDs are known to affect dogs.[18] In addition to CIPF, other described ILDs in dogs include diseases such as eosinophilic pneumonia, lymphocytic interstitial pneumonitis, bronchiolitis, obliterans with organizing pneumonia, endogenous lipid pneumonia, pulmonary alveolar proteinosis, silicosis, and asbestosis.[18] In humans, IPF belongs to an ILD subgroup named idiopathic interstitial pneumonias (IIPs). These are diseases of unknown causes resulting from damage to the pulmonary interstitium due to varying pattern of inflammation and fibrosis.[19] In dogs, such a subgroup and classification do not yet exist.

Currently, CIPF is probably the best-described canine ILD. It causes collagenous thickening of the pulmonary interstitium leading to impairment in the gas exchange.[7,8,10] Although CIPF is known to share clinical features with human IPF, the resemblance between the histopathologic pictures of human and canine disease was long in debate. Based on the recent (2013) study of Syrjä and colleagues,[10] CIPF seems to have histopathologic features of the two most common subtypes of human IIP, the usual interstitial pneumonia (UIP) and nonspecific interstitial pneumonia (NSIP). UIP is the histopathologic pattern of human IPF, and NSIP is the second most common IIP in humans and an important differential diagnosis for human IPF.[19]

CIPF is characterized histopathologically by two different patterns of interstitial fibrosis. All dogs appear to have mild-to-moderate, diffuse, mature fibrosis of the alveolar wall.[10] This pattern resembles the fibrosis pattern detected in human NSIP more than the patchy appearance of fibrosis in UIP. In addition to the mature fibrosis, most dogs have multifocal areas of fibrosis accentuation. In these areas, the fibrosis appears more severe, more cellular, and, therefore, less mature. This finding is more characteristic of human UIP than NSIP. In dogs, areas of fibrosis accentuation are either peribronchial or subpleural.[10] Honeycombing, profound alveolar epithelial changes, bronchial metaplasia of alveolar epithelium, and alveolar luminal changes, such as diffuse alveolar damage, can also be present in areas of more severe fibrosis. Fibroblast foci, very characteristic of human UIP, have not been found in dogs. Nevertheless, multifocal, scattered myofibroblasts have been detected in fibrotic