

GASTRO-OESOPHAGEAL REFLUX AND IDIOPATHIC PULMONARY FIBROSIS

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ABSTRACT. Idiopathic pulmonary fibrosis (IPF) is the most common of the idiopathic interstitial pneumonias. There is evidence of an increased prevalence of acid gastro-oesophageal reflux disease (GERD) in patients with IPF. Recent articles have focused on the potential role of chronic silent microaspiration in the pathogenesis of IPF. Aspiration is defined as the inhalation of gastric content into the larynx and lower respiratory tract. The reported use of GERD medications is an independent predictor of longer survival time in patients with IPF. These findings further support the hypothesis that GERD and chronic micro-aspiration may play important roles in the pathobiology of IPF. (*Sarcoidosis Vasc Diffuse Lung Dis* 2013; 30 Suppl 1: 37-39)

KEY WORDS: acid gastro-oesophageal reflux disease, case study, idiopathic pulmonary fibrosis, micro-aspiration, pathobiology, treatment

INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) is a chronic and progressive interstitial disease characterised by a histological and radiological pattern of usual interstitial pneumonia (UIP) (1). The aetiology of IPF is unknown but possible risk factors include smoking, environmental conditions, genetic predisposition, diabetes mellitus, and viral infections, and can be accompanied by other co-morbidities including chronic aspiration secondary to acid gastro-oesophageal reflux disease (GERD) (2-5).

Frequent in the general population, GERD is also relatively common in patients with other advanced lung diseases (6). For example, through its presumed association with micro-aspiration, several studies have reported a high prevalence of classic GERD (up to 90%) in patients with IPF (7-11). However, GERD is frequently clinically silent in pa-

tients with IPF (12) so that it is not so easy to distinguish between IPF patients with or without GERD (8).

In addition, although GERD may represent an important risk factor and contribute, in part, to the relentless and progressive nature of IPF, there are no convincing data demonstrating a clinical benefit of treatment for GERD in patients with IPF. This case study describes a patient with IPF presenting with co-existing symptoms of GERD, and discusses potential clinical management and treatment options and possible pathobiological mechanisms.

CASE REPORT

Presentation

A 61-year old male patient with IPF diagnosed according to the American Thoracic Society (ATS), and the European Respiratory Society (ERS) criteria (1) presented with worsening dyspnoea. He had a history of smoking but no occupational exposure or family history of IPF. GERD symptoms and endoscopic evidence of reflux were evident, but there were

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no connective tissue disease symptoms. Pulmonary function test (PFT) results included forced vital capacity (FVC) 65% predicted, diffusing capacity for carbon monoxide (DL_{CO}) 60% predicted, and a forced expiratory volume (FEV_1)/FVC ratio of 80%.

Clinical course

Triple-therapy with *N*-acetylcysteine, prednisone and azathioprine for IPF was initiated in 2008 and anti-reflux therapy prescribed. After a few months, the cough reduced slightly but there was no significant improvement in dyspnoea. PFTs were stabilised and anti-reflux therapy was withdrawn due to side effects (mainly constipation).

Two weeks later, the patient had worsening of dyspnoea (now at rest) but no fever, chills, or night sweats. He was admitted to a local hospital where O_2 saturation was 89-90% with 100% O_2 and then transferred to a respiratory ward in a larger hospital. Blood and sputum cultures negative but the patient was prescribed treatment with high-dose steroids and antibiotics. Bronchoscopy was not performed due to severity of illness, but other potential causes of dyspnoea (i.e. embolism or heart failure) were excluded. High-resolution computed tomography (HRCT) showed areas of peripheral and medio-basal reticulation with honeycombing and many ground-glass opacities, especially in the right lung. The presence of lesions especially in the right lung may be characteristic of IPF exacerbation related to GERD. The patient was discharged nine days later. Reviewing the clinical history, it was evident the patient had GERD that was not treated.

DISCUSSION

IPF is a heterogeneous disease manifesting as areas of peripheral and basal reticulation with honeycombing interspersed with normal lung (1). Current concepts in the pathogenesis of IPF implicate epithelial-fibroblast interactions as a result of repeated insults to the lung parenchyma by noxious stimuli (2). While the exact cause(s) of the initiating alveolar epithelial injury are unknown, postulated mechanisms include immunological, microbial, or chemical injury, including aspirated gastric refluxate (7, 13).

Despite the apparent strong association between IPF and GERD, a causal relationship is unclear. However, although the nature of the triggering and/or recurrent injury is unknown, preliminary findings support the hypothesis that chronic micro-aspiration of gastric refluxate in patients with GERD may contribute to the pathogenesis of IPF (13). Reflux is promoted by low basal pressure in the lower oesophageal sphincter and frequent relaxations, potentiated by hiatus hernia or oesophageal dysmotility. It is therefore plausible, at least in susceptible individuals, that repetitive subclinical alveolar epithelial injury in patients with GERD due to recurrent episodes of reflux of gastric contents and micro-aspiration (i.e. tracheobronchial aspiration of small amounts of gastric secretions) may lead to the development and/or progression of IPF (10).

This case study suggests an association between IPF symptom exacerbation 10-15 weeks after cessation of anti-reflux treatment for GERD. Whilst there are little convincing data demonstrating a clinical benefit of treatment for GERD in patients with IPF, the use of GERD medications (i.e. proton pump inhibitors or H_2 blockers) have been associated with lower radiological fibrosis scores and may be an independent predictor of comparatively longer survival time in IPF patients (Figure 1) (14).

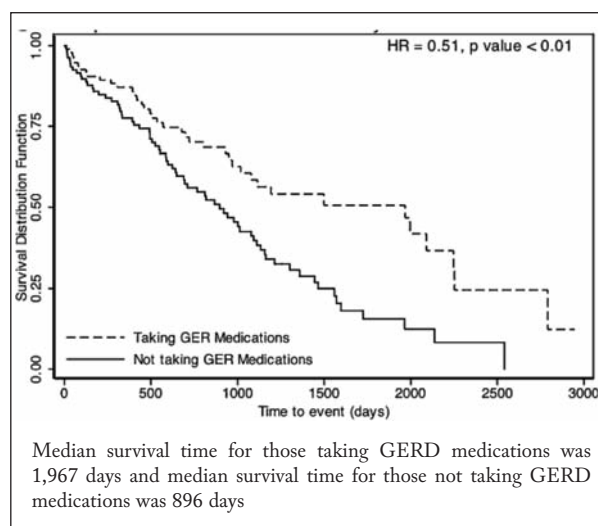


Fig. 1. Survival time estimates based on reported GERD medication use (14). Reprinted with permission of the American Thoracic Society. Copyright © 2013 American Thoracic Society. Lee JS, Ryu JH, Ellicker BM, et al. Gastroesophageal reflux therapy is associated with longer survival in patients with idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med* 2011; 184: 1390-4.

In view of significantly increased airway reflux symptoms, the putative role of gastro-oesophageal and extra-oesophageal reflux in the pathogenesis of IPF should be explored further. Investigation of non-acid reflux may also provide further insight into the mechanism of alveolar injury by gastrointestinal secretions. Further studies are also indicated to determine if optimal control of GERD has a role in the treatment of IPF.

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DISCLOSURES:

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