

Prolonged Survival in a Patient with Idiopathic Pulmonary Fibrosis Receiving Acupuncture and DHEA-Promoting Herbs with Conventional Management: A Case Report

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ABSTRACT

Introduction: Idiopathic pulmonary fibrosis (IPF) is a lethal, chronic, degenerative disease most commonly affecting the elderly population. The pathologic finding of this restrictive lung condition is excessive deposition of fibrotic tissue in the alveolar interstitium. Conventional therapies minimally alter the course of disease, and mean survival time from diagnosis is only 2 to 4 years.

Case Presentation: A 65-year-old man, diagnosed with IPF in 2007, was being monitored by a conventional pulmonologist while being treated with weekly acupuncture targeting a Chinese medicine diagnosis of spleen dampness and lung qi weakness and with botanical medicine targeting the stimulation of adrenal dehydroepiandrosterone secretion. He survived for 10 years after diagnosis.

Discussion: Studies exist linking dehydroepiandrosterone with IPF disease activity as well as acupuncture with antifibrotic activity. Larger clinical studies are needed to substantiate the link between acupuncture and/or dehydroepiandrosterone-stimulating herbs for the treatment of IPF.

INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) is a common form of interstitial lung disease. The lung interstitium is defined as the supportive connective tissue in the parenchyma of the lung between the alveolar epithelium and the pulmonary capillary endothelium.¹ Interstitial lung diseases affect the parenchymal area of the lung, impairing gas exchange, and fall under the functional category of restrictive lung diseases. In contrast, obstructive lung diseases manifest in the pulmonary airways, preventing pulmonary expiration.

IPF is a subset of a group of interstitial lung diseases called idiopathic interstitial pneumonia, with different courses, etiologies, and patterns of fibrosis. Liebow and Carrington² created 5 histologic classifications of idiopathic interstitial pneumonia, with the most common being usual interstitial pneumonia (UIP), which accounts for between 47% and 64% of cases. Complicating matters, some medical circles group different types of idiopathic interstitial pneumonia together as IPF. Discerning categories in medical literature can be difficult. For the purpose of this article, IPF will refer to the disease consistent with the UIP histologic pattern.

Patients with IPF are usually older than age 50 years, and two-thirds are diagnosed after age 60 years.¹ Disease prevalence is about 15 per 100,000 people in the US.¹ Risk factors include male sex and a history of smoking. A small percentage, less than 4%, experience a familial form of the condition.³

IPF has been found to be caused by excessive fibrotic response to alveolar epithelial damage.⁴ The pathogenesis was previously believed to be because of inflammatory-induced tissue changes; this revision explains the lack of efficacy of anti-inflammatory drugs in treating IPF.⁵ Alveolar damage induces a signal cascade from epithelial type I pneumocytes to type II pneumocytes to fibroblasts in the adjacent interstitium. The fibroblasts transform to myofibroblasts and deposit collagen.⁴ In IPF, the fibrous deposition pathway is excessive. Apoptosis of fibroblastic cells are downregulated,⁶ collagen fibers accumulate, and the interstitium thickens and hardens.⁴ Alveoli thickening reduces contractility and diffusion of gases in the parenchyma, resulting in a restrictive lung disease.

Although the pathway is well understood, the etiology of the dysregulation of the fibrotic response is not, hence the idiopathic nature of the condition. One theory suggests that injury causes damage to type I epithelium and the basement membrane of alveoli, allowing migration of fibroblastic cells from adjacent tissue into epithelium. Another theory suggests that the disease is a normal response to some chronic stimulus irritating the pulmonary tissue.⁴

Diagnosis requires all 3 of the following components: 1) pulmonary function study results indicating evidence of restrictive lung disease; 2) high-resolution computed tomography of the chest showing reticular bibasilar abnormalities with minimal ground-glass appearance, in a typical UIP pattern; and 3) exclusion of other known causes of interstitial lung disease such as asbestosis. If these clinical and radiographic parameters leave diagnostic uncertainty, a lung biopsy specimen consistent with the UIP histologic pattern is definitive; however, other diseases such as rheumatic disease, hypersensitivity pneumonitis, and pulmonary Langerhans cell histiocytosis (histiocytosis X) can present with identical histologic patterns to IPF.¹

The prognosis of IPF is grim, with a mean life expectancy of 2 to 4 years.⁷ Conventional medicine treatment focuses on palliation and prevention of respiratory exacerbation. Supportive treatments include supplemental oxygen, respiratory rehabilitation,

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and application for lung transplants, although most patients are rejected for transplant lists because of their older age. IPF is the second-most common disease indication for lung transplant. The survival rate 5 years after transplantation is only 40% to 50%.⁵ All patients with IPF are advised to receive the pneumococcal vaccine to prevent further respiratory compromise.

The course of the disease varies. Some patients follow a steady linear decline, some succumb to a rapid decline, and others experience points of acute exacerbation that launch them into rapid decline. Patients are advised to protect themselves from respiratory assaults such as upper respiratory tract infections, because an acute exacerbation could lead to death. The American Thoracic Society recommends monitoring pulmonary functional values every 3 to 6 months to assess for disease progression and prevent worsening of acute exacerbations.⁸

Because of the high morbidity and mortality of IPF compounded with the limited efficacy of conventional therapies, clinicians may consider alternative therapies that could increase quality of life and life expectancy.

CASE PRESENTATION

Presenting Concerns

A 55-year-old man presented to the pulmonology clinic in spring 2007 with a chronic dry cough and dyspnea on exertion. He had no diagnosis of any serious pulmonary condition. Minor respiratory complaints, including shortness of breath, dated to at least 2004. The organic cause of his complaints at that time was unknown. He initiated weekly acupuncture treatments in 2004, which he maintained consistently for 13 years. The acupuncture treatments focused on treating the Chinese medicine diagnosis of spleen dampness. After 1 year of weekly acupuncture, the patient noticed improvement in shortness of breath.

In 2001, 6 years before initially presenting to his pulmonologist, the patient was quite active, hiking up to 10 miles in a day, before the insidious onset of his respiratory weakness. At presentation in 2007, he was obese with a body mass index of 36.8 kg/m² and had the following diagnoses: Stage 1 hypertension, allergic rhinitis, gastric reflux, and depression that was well managed with a selective serotonin reuptake inhibitor. The patient reported no signs of infectious illness, wheezing, or dizziness and was not using supplementary oxygen. He denied a history of asbestos exposure and tobacco use. His family history was remarkable for severe asthma affecting his sister but no other respiratory illnesses. The patient was employed as an economics professor at a local university. He was single without children and lived alone.

Pulse oximetry readings (in the pulmonologist's office in April 2007) revealed an oxygen saturation of 95% at rest, which decompensated to 79% with a 6-minute walk test. Results of cardiovascular, thyroid, abdominal, genitourinary, and neurologic examinations were unremarkable. Extremities showed minor pitting edema without evidence of peripheral or central cyanosis. The pulmonologist's auscultation revealed diffuse crackles on inspiration bilaterally halfway up from the bases without prolonged expiration.

Because progressive dyspnea on exertion has many organic causes, including many types of restrictive and obstructive lung

diseases as well as autoimmune and rheumatic causes, the pulmonologist completed a thorough workup to rule out differential diagnoses. Spirometry completed in October 2007 confirmed severe restrictive lung disease revealing a predicted forced vital capacity (FVC) of 54% and a predicted diffusing capacity of the lungs for carbon monoxide of 46%, but with a forced expiratory volume during the first second of expiration (FEV₁)/FVC index of 78%. Flow loops showed no sign of obstructed airways.

The pulmonologist ordered measurement of creatinine kinase, antineutrophil cytoplasmic antibody, antinuclear antibody, anticyclic citrullinated peptide, and aldolase to assess for autoimmune activity, in addition to creatinine and serum urea nitrogen to measure kidney activity; the results from these tests were unremarkable. The complete blood cell count showed no signs of systemic infection. A normal echocardiogram ruled out compromised cardiac function.

A chest computed tomography scan confirmed structural degeneration consistent with restrictive lung tissue showing subpleural cysts, honeycombing, and traction bronchiectasis. Because different forms of interstitial lung diseases have different prognostic forecasts, the pulmonologist completed a biopsy in September 2007. The biopsy specimen revealed a UIP histologic pattern, confirming a diagnosis of IPF. The invasive biopsy procedure was undertaken because of the severity of IPF and the necessity of ruling out other nonterminal or reversible conditions. Some clinicians, however, believe that a diagnosis of IPF can be made without biopsy because high-resolution computed tomography alone has a specificity of greater than 90%.⁵

Therapeutic Intervention and Treatment

The patient initiated weekly acupuncture therapy in 2004 focusing on spleen dampness. Chinese medicine diagnosis was made by assessing the pulse and the tongue and by palpating for tender Mu points on the body. In Chinese medicine, each organ has a corresponding Mu point, which is tender when overstressed. The patient's tongue showed a thick white coating, his radial pulse expressed a slippery quality on palpation, and his Liver 13 acupuncture point (the Mu point for spleen) was tender. These signs and symptoms support a Chinese medicine diagnosis of spleen dampness. The diagnosis suggests that the spleen is not able to effectively process nutrition and fluid intake into the body, which was supported by the patient's obese body habitus. Although the focus of treatment on spleen dampness remained unchanged, specific acupuncture point selection varied week to week depending on point tenderness and the acupuncturist's discretion.

The pulmonologist placed the patient on supplementary oxygen therapy (4 L/min flow rate) for ambulation after first measuring his compromised ambulatory oxygen perfusion in April 2007. After the diagnosis of IPF in September 2007, the pulmonologist medicated him with azathioprine 50 mg, titrated up to 150 mg over 6 weeks; prednisone 60 mg, titrated down to 20 mg over 1 month; and N-acetylcysteine 600 mg 3 times daily, to boost production of antioxidants. This triple therapy was standard care at the time. The patient was not eligible for the lung transplant list because his body mass index was greater than 30 kg/m².

The pulmonologist weaned the patient off his prednisone regimen in April 2010 because of a change in the American Thoracic Society's guidelines. Comprehensive data and recommendations from the Society revealed that corticosteroids and other immunosuppressive medications did not change outcomes; in fact, they may have contributed to morbidity and mortality for patients with UIP. In September 2012, the pulmonologist discontinued azathioprine therapy after the patient experienced a psychiatric breakdown.

In March 2016, the patient initiated naturopathic adjunctive care. The naturopathic physician prescribed botanical tinctures and adjusted them every few months to meet the patient's evolving needs. The first formula was prescribed to stimulate production of dehydroepiandrosterone (DHEA). It was dosed in equal parts of *Panax ginseng*, *Rhodiola rosea*, *Schisandra chinensis*, *Dioscorea villosa*, *Glycyrrhiza glabra*, and *Epimedium grandiflorum*. He was instructed to take 15 drops in water 3 times a day.

Follow-up and Outcomes

The patient's pulmonary radiographic and functional values were monitored every 3 to 6 months under the care of

his pulmonologist. Biannual FVC measures were recorded (Appendix A, available at www.thepermanentejournal.org/files/2019/18-074-App-A.pdf). Pulmonary measures, including pulse oximetry, pulmonary function, and radiographic tissue changes, were assessed. The FVC value improved from 38% predicted at the time of IPF diagnosis in 2007 to 59% in October 2011 and steadily declined to a low of 41% in 2014. After 2014, FVC values were stable at around 40%.

In April 2010, the patient experienced an acute psychiatric breakdown involving multiple suicide attempts, and he was hospitalized and advised to take a leave of absence from work. During this period, he lost 18 kg (40 lb), reducing his risk of complications from obesity but placing him in danger of becoming cachexic. He lost any future possibility of being placed on a lung transplant list. His Chinese medicine diagnosis also shifted from spleen dampness to lung qi deficiency. Signs and symptoms that supported the new diagnosis were as follows: His body habitus was no longer obese; Lung Point 1, the Mu point for the lung, was tender; his radial pulse was less slippery and weaker on the distal right position; and his tongue no longer had a thick white coating.

Table 1. Timeline of the case

| Date (mo/d/y) | Status | Conventional therapy | Alternative therapy |
|---------------|--|---|--|
| 2004 | Patient experiences insidious onset of shortness of breath | | Weekly acupuncture initiated targeting spleen dampness |
| Mid-2005 | Patient's shortness of breath well controlled | | |
| 4/30/2007 | Thoracic CT scan: Pattern consistent with usual interstitial pneumonia; obese BMI; peripheral oxygen saturation stable at rest, decompensated with movement | Flow rate of 4 L/min supplemental oxygen used for ambulation | |
| 5/31/2007 | Results of autoimmune, electrolytes, kidney function tests, and echocardiogram within normal limits; pulmonary function test results: Severe restrictive lung disease and decrease in diffusing capacity without obstruction | | |
| 9/6/2007 | Biopsy specimen of right lung confirms idiopathic pulmonary fibrosis with usual interstitial pneumonitis histology pattern | N-acetylcysteine, 600 mg/d; prednisone taper, 20 mg every 2 wks from 60 mg/d to 20 mg/d; azathioprine, 150 mg/d | |
| 4/2/2010 | FVC and DLCO show moderate improvement since diagnosis; CXR shows moderate progression of fibrosis since 2007; psychiatric breakdown with multiple suicide attempts; massive weight loss during hospitalization | Removed from lung transplant list because of psychiatric concerns; weaned off prednisone therapy | |
| 9/10/2012 | CXR scarring and pleural thickening unchanged since 2010; moderate decrease in DLCO and FVC; patient declined to be on lung transplant list | Discontinued azathioprine regimen | Acupuncture treatment focus shifted from spleen dampness to lung qi deficiency |
| 7/31/2014 | URI causes tachypnea and hypoxemia; patient experiences decompensation at rest, a steady increase in symptoms, and a decline in pulmonary function; weight loss | Supplemental oxygen initiated at rest; oxygen flow rate increased for activity | |
| 3/24/2016 | Patient initiated naturopathic herbal treatment targeting DHEA secretion | | Tincture targeting adrenal function: Equal parts <i>Panax ginseng</i> , <i>Rhodiola rosea</i> , <i>Schisandra</i> , <i>Epimedium</i> , <i>Dioscorea villosa</i> , and <i>Glycyrrhiza glabra</i> : 15 drops in water 3x daily |
| 9/5/2017 | Increased dyspnea at rest | Oxygen increased to 8 L/min at rest and 15 L/min ambulatory | |
| 2/27/2018 | Patient found deceased at home | | |

BMI = body mass index; CT = computed tomography; CXR = chest radiograph; DHEA = dehydroepiandrosterone; DLCO = diffusing capacity of the lungs for carbon monoxide; FVC = functional volume capacity; URI = urinary tract infection.

In July 2014, the patient experienced an upper respiratory tract infection, which caused respiratory distress, tachypnea, and hypoxemia. This type of acute exacerbation could have induced a rapid decline; fortunately, the patient had discontinued the immunomodulation medication azathioprine 2 years earlier, and he was able to persevere, although his pulmonary function did not return to preexacerbation levels. After this exacerbation, the ambulatory oxygen rate was increased and the supplementary oxygen was expanded to support the patient at rest, with flow rates of 10 L/min and 4 L/min, respectively.

In March 2016, the patient began regularly seeing a naturopathic physician for botanical support. The prescribed herbal tinctures largely focused on the secretion of sex hormones from the adrenal cortex. The patient reported that he felt the tincture increased the efficacy of his acupuncture treatments regarding more ease with breathing.

In 2017, the patient's pulmonary metrics were similar to his 2014 values. Although he experienced a gradual increase in symptoms, his vital signs on September 5, 2017, did not suggest hemodynamic compromise: Heart rate of 90 beats/min, blood pressure of 106/70 mmHg, and respiratory rate of 14/min. His pulmonary metrics reflected a slight but steady decline from those at the time of diagnosis. His resting pulse oximetry reading had declined from 91% to 84%, and his FVC had declined from 54% to 45%. He compensated by increasing supplementary oxygen to 8 L/min at rest and 15 L/min ambulatory. He was able to attend to his tasks of daily living and self-report to his acupuncture, naturopathic, and conventional medical appointments.

Shortly after a missed appointment—the first in several years—and unanswered telephone calls, the patient was found deceased at his home on February 27, 2018. Our patient survived 10 years after diagnosis of IPF. A timeline of his case is shown in Table 1.

Patient Perspective

The patient provided his perspective as follows: “In 2004, I was looking for further support for my respiratory condition, and my massage therapist recommended that I try acupuncture. I was told that my life expectancy was 3 to 5 years and that Western medicine did not have further treatments that could change that. I began weekly acupuncture treatments and feel that they have held off the slow decline that accompanies pulmonary fibrosis. A couple years ago, I switched to 1 acupuncture treatment every 2 weeks and noticed that I lost pulmonary function that I have not been able to get back. Since that time, I have had weekly acupuncture and have incorporated naturopathic medicine as well. I would tell anyone with pulmonary fibrosis that they should seek additional alternative medicine for pulmonary fibrosis. I attribute my current life expectancy to the support it has brought me.” (11/27/2017).

DISCUSSION

The prognosis of pulmonary fibrosis is grim. From 20% to 40% of patients survive only 5 years.⁵ Clinicians have few to no resources at their disposal that have proved effective for IPF.

We chose the pulmonologist's diagnosis of IPF in 2007 as the date of origin of the disease. One may be tempted to trace the origin of the patient's condition further back to the dyspnea he began to experience in 2004, for which he initiated acupuncture. Because of a lack of conventional medical records from 2004, linking his dyspnea at that time to IPF would be speculative. Our patient nevertheless beat the odds by surviving at least 10 years with IPF, which should pique clinicians' curiosity to investigate his unique treatment management.

The triple therapy of N-acetylcysteine, azathioprine, and prednisone that the pulmonologist prescribed in 2007 was the standard of care at the time. Since that time, the medical community has moved away from the inflammatory pathogenesis of IPF to a fibrotic deposition hypothesis. The triple therapy has been shown to increase morbidity and mortality compared with placebo in at least 1 study.⁹ Since 2015, results of research surrounding nintedanib, a tyrosine kinase receptor blocker that prevents fibrogenic growth factors, have been promising. One study showed this medication halves the rate of decline of FVC compared with placebo.⁷ The therapy, researched only in patients at the mild or moderate stage of IPF, was not indicated for this patient.

Two treatment modalities for IPF that the patient used show promise for future research: *Glycyrrhiza glabra* (licorice root) and acupuncture. The medical literature has shown an indirect relationship between IPF and licorice root. Licorice has been shown to increase salivary levels of the parent sex hormone DHEA,¹⁰ and DHEA has been shown to be decreased in patients with IPF compared with control.⁶ In vitro, DHEA has also been shown to decrease both TGFβ1—a signaler for collagen production in IPF pathogenesis—and caspase-9, an intrinsic pathway signaler for fibroblast apoptosis.⁶ On the basis of these findings, a conceptual model worthy of further research is that DHEA modulates pulmonary fibrotic deposition, which is a process not well regulated in IPF.

A review of medical literature also revealed some study findings associating acupuncture with treatment of fibrotic tissue changes. One study showed reduced levels of serum markers for fibrotic deposition in rats with hepatic fibrosis compared with control.¹¹ Another murine study corroborated the reduction in serum markers in acupuncture-treated rats with induced hepatic fibrosis compared with control. The study corroborated the serum markers with tissue biopsy confirming the results; however, it should be noted that the group in the second study was also treated with curcumin extract.¹² Because the underlying mechanism causing the abnormal fibrotic tissue remodeling in IPF currently eludes biomedicine,⁴ the medical literature can at best extrapolate from other fibrotic conditions the mechanism by which acupuncture regulates fibrotic remodeling in IPF.

The medical literature already contains other case studies in which patients with IPF experience reduced symptoms and improved pulmonary function with regular acupuncture therapy.¹³ Clinicians may consider referring patients with IPF for adjunctive acupuncture and/or herbal therapy on the basis of the merits of this case and the other studies cited; however, larger clinical studies should be established to further test the efficacy of these therapies for treating IPF. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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