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Idiopathic Pulmonary Fibrosis: Understanding Has Led to Exciting Treatments

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Introduction

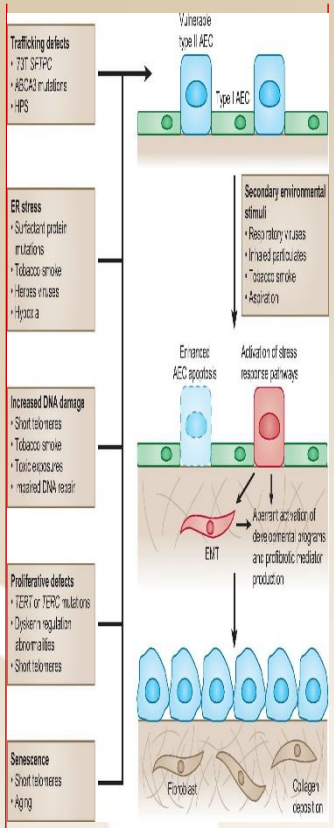
Pulmonary fibrosis can be described as an excessive amounts of fibrous connective lung tissue in the lung. Idiopathic pulmonary fibrosis(IPF) is the most common form of interstitial lung disease(ILD). When an obvious cause cannot be determined, a diagnosis of Idiopathic pulmonary fibrosis is made. The mean survival for patients is approximately 3-5 years from time of diagnosis. IPF is found primarily in men over 50 years of age, with a history of cigarette smoking with concurrent environmental and occupational inhalation exposures(Leslie, 2011, p. 592). Pulmonary fibrosis has been identified by early pathologists at the beginning of the last century. During autopsy, the signature "honeycombing" of a shrunken, cystic and fibrotic lungs were first identified.

IPF was first thought to an inflammatory disorder which was treated with corticosteroids and cytotoxic medications. New understanding of IPF and the pathophysiology have shaped new treatments. "Current concepts suggest that the disease results from aberrant reparative response to alveolar epithelial cell injury characterized by migratory proliferation, activation of fibroblasts and secretion of excessive amounts of extracellular matrix components, leading to scarring of the lungs, architectural distortion, and irreversible loss of function" (Tzouvelekis, Bonella & Spagnolo, 2015, p.359). Working on a vascular thoracic floor, many patients are admitted with a diagnosis of IPF.

Presentation of Case

A 76 year old man was admitted with complaints of increased shortness of breath and is now requiring increased amounts of home oxygen. He is having an elective VATS (video-assisted thoracscopic surgery) lung biopsy which showed interstitial pneumonitis. Since he has no acute (medicine, radiation) or identifiable cause for pulmonary fibrosis, he is diagnosed with idiopathic pulmonary fibrosis. Due to his advanced age he is not a candidate for lung transplantation(Sheppard, 2013, p. 1055). What treatment is available for this patient? What is his prognosis? What will be his disease progression?

Signs and Symptoms of IPF



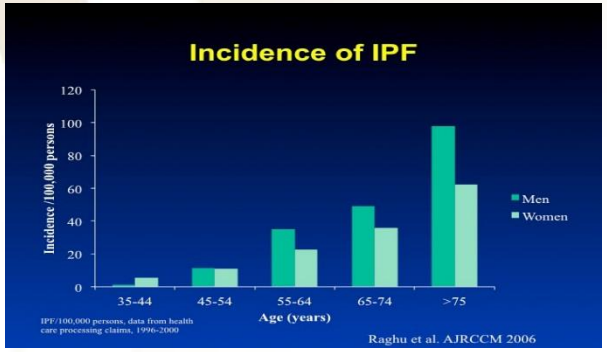
Signs and Symptoms of IPF

According to the National Lung, Heart and Blood Institute (2011), the most common symptom of IPF is shortness of breath. Initially a patient will have shortness of breath with exercise, but as the disease progresses a patient with have shortness of breath at rest. The other late and secondary symptoms are: increased breathing rate, unintended weight loss, fatigue, malaise, aching muscles and or joints, and clubbing of the fingers. IPF causes scarring and symptoms similar to other common lung ailments such as COPD (Chronic Obstructive Pulmonary Disease), so early and correct diagnosis are very important to patients and families.

Imaging will show traction bronchiectasis, thickening interlobular septae, and sub pleural honeycombing. When all the three above are present with no connective tissue disease or environmental exposure, then a confident diagnosis of IPF can be made (Noble, Barkauskas, and Jians, 2012, p. 2756).

Misdiagnosis

Until recently, idiopathic pulmonary fibrosis was misdiagnosed and treated with medications which did not improve the prognosis. Improvement of understanding of IPF has led to the first approved drugs to slow the progression of the disease. Studies have been performed looking at medication and pulmonary rehabilitation to improve quality of life and outcomes for pulmonary fibrosis patients.



Underlying Pathophysiology of IPF

"Idiopathic pulmonary fibrosis (IPF) is a deadly lung disease with few therapeutic options. Apoptosis of alveolar cells, followed by abnormal tissue repair characterized by hyperplastic epithelial cell formation, is a pathogenic process that contributes to the progression of pulmonary fibrosis. However the signaling pathways responsible for increased proliferation of epithelial cells is poorly understood"(Weng et al. 2014, p. 1402).

IPF has been linked to:

* Cigarette smoking
* Environmental exposures
* Pharmacological Side effects
* Medical Diseases
* Virus or microbes

Understanding of role of the initial injury and the subsequent aberrant cellular repair has opened up new theories and treatments for IPF. Multiple studies have been undertaken to find a singular response to the initial injury, but multiple cell and responses may be in play with IPF(Ryu, et al, 2014, p. 1132).

Genetic transmission

- Genetics transmission may happen in 5% of all IPF cases
- Transmission is autosomal dominant with variable and reduced penetrance.
- Genetics studies have identified mutations only expressed in lung epithelial cells(Noble et al., 2012, p. 2757).
- A specific gene, *MUS5B* has been identified in 38% of patients with IPF
- *MUS5B* is only expressed in bronchiolar, not epithelial cells but the discovery shows possibility of biomarkers (Flynn, Baker, & Kass, 2015, p. 21).
- Mormon death certificate database may show larger genetic component(Scholand, Coon, Wolff, & Cannon-Albright, 2013, p. 480)

Updated Theories of IPF

"Several lines of evidence have emerged implicating a combination of environmental, age-related and genetic factors that coalesce to create alveolar epithelium that is susceptible to injury from either unknown endogenous factors or exogenous insults such as viral infection or micro aspiration" (Noble, et al., 2012, p. 2758).

Tyrosine Kinase Role in IPF

- Epithelium-mesenchymal cross talk and destruction of mesenchymal expansion shows the attempt to repair damage by alveolar epithelial type 2 cells (AE2C) that release growth factors, cytokines and coagulants. Tyrosine kinase has been linked to IPF in recent studies (Noble, et al., 2012, p. 2759).
- The discovery of the role of tyrosine kinase in IPF has led to the development of the first FDA approved drugs in 2014
- Tyrosine kinase inhibitors: Nintedanib and Pirfenidone

Significance of Patho

- Tyrosine Kinase is just one isolated factor released in the complicated pathophysiology of IPF
- "The factors promote mesenchymal expansion and activation, leading to accumulation of matrix-producing and invasive fibroclasts and myofibroclasts" (Noble, et al., 2012, p. 2759).
- Mesenchymal expansion and destruction leads to the distinctive honeycombing effect of pulmonary fibrosis and poor oxygen/carbon dioxide exchange in alveolar cells.
- The damage is non-reversible and leads to the poor prognosis associated with IPF
- Three studies published in 2014 showed when patients were given either nintedanib or pierfenidone had significant lower rate of decline of FVC versus patients receiving placebo at 52 weeks (Mandel et al., 2014, p. 117).
- The research shows the first substantial medical treatment of IPF
- Results of the three studies must be examined and looked at much closer
- Even with exciting research results two limitations identified by the study authors need to be taken into account
- First, the studies did not look at the beneficial effects past 52 weeks or the effect on mortality and morbidity
- Second, the authors caution both drugs do not cure IPF, only slowing the progression of the disease
- The hope would be slower progression of the disease will help lead to more time to find a lung transplant donor for patients with IPF. Lung transplant is the only known curative treatment today

Nursing Implications

- Nurses with updated evidence based practice information on IPF can be an invaluable source of education for patients and family.
- New theories about IPF would contradict recent nursing education and treatment of patients
- Studies have been undertaken in recent years show pulmonary rehabilitation has been effective in COPD patients, but the benefit has been less clearly shown with IPF measured by levels of activity and health care quality of life (Gaunaurd, et al., 2014, p. 1872).
- With no curative or many treatment options, any rehabilitation should be studied.
- 2014 study of 21 IPF patients in a randomized control trial between groups of organized pulmonary rehab versus a control group of no organized rehab showed "those pulmonary rehabilitation benefits patients with IPF by enhancing their level of physical activity and by significantly reducing the disease's symptom burden" (Gaunaurd, et al., 2014, p. 1878).

Conclusion

- IPF can be similar in symptoms and presentation with other lung diseases
- The sooner IPF can be diagnosed has been shown to reduce stress reported by patients with IPF (Duck, et al., 2014, p. 1055).
- IPF is rare when compared to COPD, care must be taken to differentiate between the two diseases
- Time is critical for IPF patients to be evaluated for possible lung transplantation. New drugs and interventions need to be studied in this population
- Pathophysiological understanding of this disease has lead to exciting treatments and most of all some hope for patients and families dealing with this terrible diagnosis

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