Investigation of Pulmonary Fibrosis in Corrales, New Mexico: 2010 - 2011

Background

In August 2010, a New Mexico resident contacted the New Mexico Department of Health (NMDOH) with concerns about "a cluster of cases of pulmonary fibrosis in Corrales" with an unknown cause. What follows is a description of the condition as well as a summary of the investigation.

Pulmonary fibrosis is a serious disease that causes progressive scarring of the lung tissue. Pulmonary fibrosis of unknown cause, also known as idiopathic pulmonary fibrosis (IPF), is the most common type of interstitial lung disease (ILD). ILD is the generic term used to describe a number of conditions which primarily affect the lung parenchyma in a diffuse manner. They are characterized by chronic inflammation and/or progressive interstitial fibrosis, and share a number of clinical and radiological features such as dyspnea on exertion, non-productive paroxysmal cough, abnormal breath sounds, abnormal high resolution CT scan, and restrictive pulmonary spirometry with impaired gas exchange.

The ILDs can be broadly grouped into three categories (Longmore et al. 2007):

1) Conditions with a known etiology (e.g. asbestosis, silicosis, tuberculosis, allergic alveolitis)
2) Conditions with systemic disorders (e.g. lupus, ulcerative colitis, rheumatoid arthritis)
3) Conditions with an unknown cause (e.g. IPF, cryptogenic organizing pneumonia)

IPF has a median survival of less than 3-5 years following diagnosis (Harari & Caminati, 2010). It is the most common of the idiopathic interstitial pneumonias, with a prevalence of 13-20 per 100,000 people in the general population. Males are affected more often than females, and approximately 75% of patients are older than 60 years of age at presentation. It should be emphasized that IPF is very similar to other well-defined diseases, such as asbestosis, the connective tissue diseases, and a number of other conditions. Therefore, known causes must be ruled out before the term/label of "idiopathic" is used (Brashers, 2006).

Based on a population-based registry of patients with ILDs[1] that was established in 1988 in Bernalillo County, New Mexico, the overall prevalence of ILDs for the period of 10/01/1988 to 09/30/1990 was 80.9 per 100,000 in males and 67.2 per 100,000 in females (Coultas et al., 1994). The annual incidence rate (rate of new cases diagnosed) was 31.5 per 100,000 in males and 26.1 per 100,000 in females. The prevalence of IPF, a subset of ILD, was 20.2 per 100,000 for males and for females it was 13.2 per 100,000.

The diagnosis of IPF requires clinical, radiographic, and histopathological evaluations. Secondary causes of pulmonary fibrosis, including collagen-vascular disease, chronic hypersensitivity pneumonitis, adverse drug reactions, granulomatous diseases, and pneumoconiosis must be excluded.

[1] Coultas et al. (1994) define IDLs as "a heterogeneous group of disorders that comprise more than 130 entities with some diagnoses commonly encountered by pulmonary physicians in the United States."

Methods

In August 2010, the Epidemiology and Response Division of the NMDOH began investigating idiopathic pulmonary fibrosis cases in Corrales through the development of a case definition, collection of medical records, analysis of medical records against the case definition, and the calculation of an idiopathic pulmonary fibrosis prevalence rate in Corrales.

First, NMDOH created a case definition for idiopathic pulmonary fibrosis. This definition was based on the American Thoracic Society/European Respiratory Society's criteria for diagnosis of idiopathic pulmonary fibrosis (Appendix). This definition was used to categorize the IPF status of each case as confirmed, probable, suspected, or not IPF.

Next, a list was gathered of current or former residents of Corrales who either self-identified as having pulmonary fibrosis or were previously identified through the *Corrales Comment* as having pulmonary fibrosis. A request for medical records was made for each of these residents. This process took several months since some residents had died or moved out of state, making record acquisition more laborious.

Finally, data were analyzed and the prevalence of IPF in Corrales was calculated.

Results/Discussion

A total of ten potential cases of IPF were identified. The age range of the cases was 47-76; six were females and four were males; four were deceased. Of these, all had some type of lung disease. However, only one case was confirmed as having IPF. Of the remaining nine potential cases, six were classified as not IPF based on the identification of an alternate diagnosis such as chronic obstructive pulmonary disease (COPD), sarcoidosis, and hypersensitivity pneumonitis. One case was excluded because the person had developed pulmonary fibrosis before moving to New Mexico. NMDOH did not have enough information to confirm the IPF case status for two potential cases, both of which were deceased. Therefore, these two cases were classified as suspected IPF.

Based on data from the 1990 and 2000 censuses, the Corrales population is 6,394 (www.census.gov). With one confirmed IPF case, the rate is 15.6 per 100,000 population. This is within the range of IPF prevalence found by Coultas et al. (1994) for Bernalillo County from 10/01/1988 to 09/30/1990 (20.2 per 100,000 for males and 13.2 per 100,000 for females.)

Conclusions

NMDOH identified a heterogeneous group of lung disease in Corrales due to various causes. An IPF cluster was not identified.

References

1. Brashers, V.L. 2006. Alterations of pulmonary function. In McCance, K.L. and S.E. Huethner, editors: Pathophysiology: The Biologic Basis for Disease in Adults and Children, Fifth edition, Philadelphia, Elsevier Mosby, p. 1216.
2. Caminati, A and S Hariri. 2010. IPF: new insight in diagnosis and prognosis. Respiratory Medicine 104(S1): S2-S10.
3. Coultas DB, Zumwalt RE, Black WC, Sobonya, RE. 1994. The epidemiology of interstitial lung diseases. American Journal of Respiratory and Critical Care Medicine 150: 967-972.
4. Longmore M, Wilkinson IB, Turmezei T, and CK Cheung, editors. 2007. Oxford Handbook of Clinical Medicine. 7th Edition. Oxford University Press, New York.

Appendix: Case Definition for Idiopathic Pulmonary Fibrosis (IPF)

1. **Does Case Have an Interstitial Lung Disease (ILD)?** Each case was first evaluated to determine if it met the clinical and pathological features of ILD. If it did not, it was excluded from analysis.

   Interstitial Lung Disease Definition: A number of conditions that primarily affect the lung parenchyma in a diffuse manner.

   A. Clinical Features**:**
   Dyspnea on exertion, non-productive paroxysmal cough, abnormal breath sounds, abnormal CXR or high resolution CT scan, restrictive pulmonary spirometry with reduced DLCO.

   B. Pathological Features**:**
   Fibrosis and remodeling of the intersitium, chronic inflammation, hyperplasia of type II epithelial cells or type II pneumocytes

   C. Classification Categories:
   i. *Conditions with a known etiology:*
   -Occupational/Environmental e.g. asbestosis, berylliosis, silicosis
   -Drugs: nitrofurantoin, bleomycin, amiodarone, sulfasalazine, busulfan
   -Hypersensitivity reactions e.g. extrinsic allergic alveolitis
   -Infections e.g. TB, fungi, viral
   ii. *Conditions associated with systemic disorders:*
   -Sarcoidosis
   -Rheumatoid Arthritis, SLE, Systemic Sclerosis, MCTD, Sjogren's syndrome
   -Ulcerative Colitis, RTA, Autoimmune Thyroid Disease
   iii. *Conditions with an unknown cause*:
   -IPF/CFA
   -Cryptogenic Organizing Pneumonia
   -Lymphocytic Interstitial Pneumonia

2. **If Case has ILD, Does It Meet Idiopathic Pulmonary Fibrosis (IPF) Definition?** Once a case was defined as having an ILD, it could be evaluated to determine if it met the criteria for idiopathic pulmonary fibrosis (IPF). The definition for IPF is based on the American Thoracic Society/European Respiratory Society criteria for diagnosis of IPF in absence of surgical lung biopsy.

   IPF diagnosis requires clinical findings compatible with ILD in combination with either characteristic radiologic findings (probable) or a pathologic diagnosis of usual interstitial pneumonia (UIP) on surgical lung biopsy (confirmed).

   A. Major Criteria
   i. Exclusion of other known causes of ILD such as certain drug toxicities, environmental exposures, and connective tissue diseases
   ii. Abnormal pulmonary function studies that include evidence of restriction (reduced VC[2], often with an increased FEV1/FVC ratio) and impaired gas exchange [increased P (A–a) O2[3], decreased PaO2 with rest or exercise or decreased DLCO[4]]

[2] VC= vital capacity.

iii. Bibasilar reticular abnormalities with minimal ground glass opacities on HRCT[5] scans
iv. Transbronchial lung biopsy or BAL[6] showing **no** features to support an alternative diagnosis

B. Minor Criteria
i. Age > 50 yr
ii. Insidious onset of otherwise unexplained dyspnea on exertion
iii. Duration of illness > 3 mo
iv. Bibasilar, inspiratory crackles (dry or "Velcro"-type in quality)

C. Case Classification

In the immunocompetent adult, the presence of **all** of the major diagnostic criteria as well as at least **three** of the four minor criteria increases the likelihood of a correct clinical diagnosis of IPF. Potential cases are classified in the following manner:

i. *Confirmed:* Clinically compatible with ILD and has a surgical lung biopsy (such as through video-assisted thoracoscopic surgery) consistent with usual interstitial pneumonitis.
ii. *Probable:* Meets all of the major diagnostic criteria (including typical HRCT for IPF) and at least three of the four minor criteria, but does not have a surgical lung biopsy.
iii. *Suspected:* Meets at least three of the major criteria (but no HRCT or the HRCT is inconclusive for IPF) and meets at least three minor criteria, but has no surgical lung biopsy.
iv. *Not IPF:* If none of the above applies, the condition is not IPF.

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[3] P (A–a) O2= alveolar–arterial pressure difference for O2

[4] DLCO = diffusing capacity of the lung for CO

[5] HRCT= high-resolution computerized tomography

[6] BAL = bronchoalveolar lavage

References:

1. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonia. 2002. American Journal of Respiratory and Critical Care Medicine 165:277-304.
2. National Institutes of Health web page (www.nhlbi.nih.gov).
3. Raghu G, Weycker D, Edelsberg J, Bradford W, Oster G. 2006. Incidence and prevalence of idiopathic pulmonary fibrosis. Journal of Respiratory and Critical Care Medicine 184: 810-816.
4. Rosas IO, Richards TJ, Konishi K, Zhang Y, Gibson K, et al. 2008. MMP1 and MMP7 as potential peripheral blood biomarkers in idiopathic pulmonary fibrosis. PLoS Medicine 5(4): 623-633.
5. Armanios M, Chen J, Cogan JD, Alder JK, Ingersoll RG, Markin C, Lawson WE, Xie M, Vulto I, Phillips JA, Lansdorp PM, Greider CW, and JE Loyd. 2007. Telomerase mutations in families with idiopathic pulmonary fibrosis. New England Journal of Medicine 356: 1317-26.
6. Jastrzebski D, Gumola A, Gawlik R, J Kozielski. 2006. Dyspnea and quality of life in patients with pulmonary fibrosis after six weeks of respiratory rehabilitation. Journal of Physiology and Pharmacology 57 (S4): 139-148.
7. Nogee LM, Dunbar AE III, Wert SE, Askin F, Hamvas A, Whitset JA. 2002. Mutations in the surfactant protein C gene associated with interstitial lung disease. 2002. Chest 121 (3 suppl): 20S-21S;
8. Coultas DB, Zumault RE, Black W, Sobonya RE. 1994. The epidemiology of interstitial lung diseases. American Journal of Respiratory and Critical Care Medicine 150: 967-72.
9. King TE Jr. 2005. Clinical advances in the diagnosis and therapy of the interstitial lung diseases. American Journal of Respiratory and Critical Care Medicine 172: 268–279.
10. Nishiyama O, Kondoh Y, Kimura T, et. al. 2008. Effects of pulmonary rehabilitation in patients with IPF. Respirology 13; 394-399.
11. Ferreira A, Garvey C, Conners G, Hilling L, Rigler J, Farrell S, Cayou C, Shariat C, and HR Collard. Pulmonary rehabilitation in interstitial lung disease: benefits and predictors of response. 2009. Chest 135: 442.