Progressive Massive Fibrosis

Abstract
A multi-faceted overview of the lung disease Progressive Massive Fibrosis (PMF) is presented. The various characteristics of this disease such as origins, progression, symptoms, diagnosis, and treatment will be outlined. Protective measures involving the respiration of microscopic dust particles and recent increases in disease prevalence are discussed. A case report involving a janitorial worker who presented with PMF will also be reviewed.

Introduction
Progressive Massive Fibrosis is the most advanced and debilitating form of lung disease found among laborers in respirable dust industries.\(^1\)\(^-\)\(^5\) PMF is most notable for the formation of large mass-like conglomerates within the lungs. These are generally located in the upper lung lobes and are associated with radiating strands or fibers that protrude from the mass itself.\(^2\)\(^,\)\(^3\) This disease is most often associated with certain pneumoconioses, particularly Coal Worker’s Pneumoconiosis (CWP) and silicosis; although, pneumoconiosis and the progression to PMF may arise from any dust-producing industry.\(^1\)\(^-\)\(^7\) Similar mass-like densities have been occasionally described with other diseases such as cancer. PMF is a disease that is completely preventable and potentially fatal.\(^1\)\(^,\)\(^2\)\(^,\)\(^4\)

Anatomy of the Lungs
As tiny particles are inhaled through the mouth or nose, they pass through various tube-like structures. The particles are filtered by the mucous in the nasal cavity and pharynx. Inhaled air and particles then travel through the trachea to a bifurcation which creates the two main-stem bronchi. These bronchi then divide smaller and smaller into branches called bronchioles. The bronchioles eventually end in clusters of microscopic air sacs called alveoli. Within the alveoli, oxygen from inhaled air is absorbed into the blood. At the same time, carbon dioxide travels from the blood to the alveoli where it can be exhaled. This transfer is called diffusion and is achieved through the spontaneous movement of gases.
**Disease Process and Progression**

Pneumoconiosis disease of the lungs come from the simple inhalation of microscopic dust particles, and is generally characterized by those particles arising from silica and coal mining industries.\(^1\) Much like a pearl is formed within a clam, a particle of dust deposited in the alveolar liquid of the lung becomes encapsulated; immune responses of the human body begin. If the encapsulated particle is then unable to be dislodged, fibrotic strands will form to further enclose the infiltrating dust. These fibrous coverings have slight variances depending on the particle introduced into the tissue.\(^8\)

Inhaled particles are engulfed by alveolar macrophages that cannot digest the material. Instead, the infiltrating dust damages the lysosomal membranes of the alveoli which triggers the release of proteolytic enzymes into the cytoplasm. This leads to the eventual death of the macrophage. Continual exposure to such particles results as an alteration in the macrophage function. Release of inflammatory cytokines is then triggered which stimulates collagen synthesis and production of antibodies against collagen. These anticollagen antibodies stimulate fibroblasts to then produce more collagen which eventually leads to nodule formation.\(^2\) A typical pneumoconiotic nodule has the following characteristics:

- Central zone with whorls of dense, hyalinized fibrous tissue.
- Midzone with concentrically arranged collagen fibers similar to onion skinning.
- Outer zone with randomly orientated collagen fibers mixed with dust-loaded macrophages and lymphoid cells.\(^2\)

There is little difference among pneumoconiotic diseases. Silicosis is an occupational lung disease caused by the inhalation of crystalline silica.\(^2\) A particle of silica introduced into lung tissue is known as Silicosis; whereas a particle from respirable coal dust is known as CWP. These are both characterized as slowly progressing nodular fibrosing pneumoconiosis diseases.\(^2\)

PMF is a complication that arises from both CWP and Silicosis; it is recognized when fibrotic nodules coalesce and expand to form large solid lesions.\(^1,2,7\) Massive fibrosis of the lung results in a stiff and nondistensible lung with an increased elastic recoil. As this disease worsens, adjacent lung tissue retracts toward the lesions. Alveoli and blood vessels are subsequently destroyed, and airways become distorted as lung volume is lost from retraction.\(^1\) PMF the most debilitating and potentially fatal stage of particle inhalation diseases.\(^1,2,3\)
Risk Factors

Those who work in industries such as mining, stone working, sandblasting, surface drilling, tunneling, silica flour milling, ceramic manufacturing, and so forth are predisposed to develop any form of pneumoconiosis. The type of job performed by miners, such as roof-bolting and the operation of constant mining machines put workers at higher risk. These laborers are those who most commonly contract lung disease due to greater exposure. It has also been proposed that advances in mining equipment may increase risk of disease contraction since newer machines produce smaller dust particle sizes. Additionally, whether a miner works underground or on the surface is a contributing factor. Workers who are confined underground, with increased dust levels and limited air movement, have greater risk of disease than those above ground.

Recently, miners from 15 states participated in a voluntary consensual study. It was found that the prevalence of CWP was higher in 3 of those states. Percentages of miners with CWP in those states are: Kentucky, 9.0%; Virginia, 8.0%; West Virginia, 4.8%. Miners in these states were, on average, younger and had less mining tenure compared to the 12 other states. Also, it is reported that 46.7% of small mines, those with fewer than 100 employees, are located in these 3 states.

Due to exposure from many sources and industries, silicosis is currently the most prevalent chronic occupational lung disease in the world. Not surprisingly, silica is known to be more toxic than coal dust; as such, it causes a greater inflammatory and fibrotic response in the lung. It is well understood that inhalation of any form of dust particle is harmful. Overall, risk is assessed by the amount of respirable dust within each environment and the workers age, or work tenure, in the given industry.

Coal Worker Protection: The Law of 1969

Implementation of effective occupational health standards has always been a tortuous process with the United States government. In the 1930s, the US Public Health Service played a major role in conceptualizing coal mine dust as virtually harmless. It was claimed that the mixed particulate matter produced from coal mining was merely a nuisance, not a serious hazard. However, these claims made by government officials were quickly disproved by scientific advances and autopsy comparison. In 1969 the Coal Mine Health and Safety Act became law
which was aimed to protect coal miners from physical harm, such as cave-ins, and pathological harm from dust exposure.\textsuperscript{5} The Federal Coal Mine Health and Safety Act was signed under duress by President Nixon in December of 1969. This granted immediate reduction in permissible mine dust exposure to 3.0 mg/m\textsuperscript{3}.\textsuperscript{8} After nearly four decades of denial and dismissal of the reality of dangers from coal exposure, the government finally opened its eyes to their own negligence. The United States had set the strictest dust-control policy for coal mines of any nation in the world.\textsuperscript{8}

Since complete implementation in 1972, coal mines within the United States have been required to comply with the permissible limit of 2.0 mg/m\textsuperscript{3} for respirable dust.\textsuperscript{1,8} The goal of this limit was to decrease the overall incidence of CWP.\textsuperscript{1,8} It also aimed to prevent the most advanced and lethal stages of CWP from developing. Operators of these mines are required to monitor respirable dust exposure levels in order to demonstrate compliance with the law. Along with the dust reports, mines were also mandated that they must offer periodic radiographic health surveillance.

After the law of 1969, dust levels reported for enforcement purposes declined.\textsuperscript{1} As expected, it was indicated through surveillance radiographs that there was a progressive decline related to the prevalence of advanced CWP among miners who had started working after implementation of the act.\textsuperscript{1} This decline continued until approximately 2001, when an increase in all types of CWP began to be observed.\textsuperscript{1,9}

In a study performed by Laney et al in 2009, it was proved that the prevalence of CWP and PMF had increased in the last decade. This has occurred amidst the stable reports of respirable dust. The greatest increase in disease prevalence was noted in small mines. PMF has been observed in miners as young as 40 years of age.\textsuperscript{3} Mine size is also associated with disease incidence, though it is not the main issue. The issue is due to factors associated with size. Small mine size brings with it limited resources and consequently a limited knowledge of dust reduction and elimination; the equipment required to properly do so. Thus, employees of small mines are presented with lower quality standards and fewer educational opportunities. Alarmingly, progression from CWP to PMF was noted as early as 5 years from the last normal chest radiograph in some miners.\textsuperscript{1} These results starkly emphasize the need for improved dust control measures and the importance of continual active health surveillance of those exposed to respirable dust.
Symptoms and Clinical Presentation

Since PMF is the most severe and advanced pneumoconiotic disease, it is usually not the first diagnosis for laborers in dust-producing industries. Most patients present as normal walking-talking people. This may be due to the fact that no major symptoms are reported with early pneumoconiosis; uncomplicated pneumoconiosis does not usually decrease activity or life expectancy.\(^1\) Patients with advanced pneumoconiosis are prone to develop mild to severe complications, such as:

- Infection.
- Tuberculosis.
- Lung cancer.
- Progressive massive fibrosis.
- Chronic Obstructive Pulmonary Disease.
- Chronic bronchitis.
- Emphysema.
- Cor pulmonale.
- Broncholithiasis.
- Tracheobronchial compression by enlarged lymph nodes.\(^2,3,10\)

Pleural involvement in silicosis is rare.\(^2\) Airflow limitation, sputum production, wheezing, pulmonary hypertension, and death from respiratory failure or heart failure can occur in PMF, even without further dust exposure.\(^1-3,6,7\) A non-smoking 33-year-old presented with progressive breathlessness, dry cough, and pleuritic chest pain; all of which are symptoms suggesting an advancing chronic pneumoconiosis.\(^2\) Further complicating the decreased lung volume caused by large nodules, increased elastic recoil and nondistensibility of the lung also results in alveolar defects and decreased lung capacity.\(^2\)

In most cases, PMF is not always an alarming disease for patients until diagnosed through chest radiographs; however, early detection may be possible from the aforementioned symptoms. The average progression from any pneumoconiosis to PMF occurs at a staggering rate of 12.2 years from the last normal chest radiograph.\(^1\) This may not seem to be a staggering figure; however, screening exams are only offered once every 5 years.

Screenings for at risk persons must be provided by law. In fact, an enhanced surveillance program was initiated in 2005 by the National Institute for Occupational Safety and Health for
underground coal miners. This program was implemented after a notable increase in disease prevalence.\textsuperscript{3} However, very few miners, as little as 31\%, utilize this service which is not considered mandatory for workers who do not wish to pursue screening examinations.\textsuperscript{1,8} Moreover, many miners are unaware that they have pneumoconiosis since it often presents without symptoms in the less severe stages of the disease.\textsuperscript{1} Screening examinations generally include chest X-rays, pulmonary function tests and work history.\textsuperscript{1-3,6,7}

Lung biopsy is also an option but rarely performed for the diagnosis of pneumoconiotic disease; as it is easily detected by occupational history and radiological features. However, a case report stated that core samples were tested post-mortem. In this case, microscopic white spots of the sample represented silica crystals. Further microscopy revealed that those silicotic nodules contained some dust laden macrophages and were primarily composed of lymphocyte inflammatory cells.\textsuperscript{2}

**Pulmonary Function Testing**

Current findings indicate that severe occupational lung disease develops in many current US coal miners during their productive working years. These reports provide further evidence that the rapidly progressing form of pneumoconiosis, PMF, often leads to severe lung impairment. Miner lung function declined at a considerably accelerated rate compared to those nonsmoking and smoking nonminers of similar age. Nonsmokers had an average lung volume decrease of 37mL/y, and those who smoked averaged 48 mL/y; compared to the 87 mL/y decrease in lung volume of miners with advanced pneumoconiosis.\textsuperscript{1}

**Plain Radiography**

Plain film radiography is a simple and effective diagnostic tool that provides excellent images for easy detection of lung nodules. These nodules are generally in the upper-lung zones.\textsuperscript{2,3,7} Uncomplicated and less severe pneumoconiotic nodules measure <10mm in size; whereas PMF is diagnosed by fibrotic-appearing nodules that measure >10mm in size (See Figure 1).\textsuperscript{1-3,7}

In order to properly diagnose the difference among pneumoconiosis disease, a proper history from the patient must be acquired; however, silicotic masses occasionally present with calcifications. As PMF occurs in the upper lobes, its presence is sometimes described as an
“Angel’s Wing” appearance (See Figure 2). Chest radiographs of chronic silicosis generally show bilateral, diffuse, well-defined large nodular opacities.

**Computed Tomography**

CT is the second yet most effective method of conclusively diagnosing PMF. CT Thorax and CT Pulmonary Angiograms are performed to better demonstrate disease prevalence and its severity. The mass-like areas of lung opacification are most readily viewed with CT. PMF masses are associated with radiating strands, and commonly contain air bronchograms and calcifications. These mass-like regions are also able to shrink over time and tend to move towards the hilar regions. However, cancerous nodules within the lungs may, at times, also appear as PMF.

**Magnetic Resonance**

Magnetic resonance imaging is also very effective at imaging nodules. However, it is most helpful when distinguishing between progressive massive fibrosis and lung cancer in questionable circumstances. Lung cancer typically appears as T2 bright, whereas PMF appears as T2 dark when compared to skeletal muscle. The most common MRI appearance are regions which have following signal characteristics:

- **T1** - iso hyper-intensity
- **T2** - hypointensity

Areas of internal high T2 signal with either rim enhancement or no enhancement may also be seen. MRI of the lungs can be somewhat troublesome due to MRCP exams requiring the use of bellows and respiratory gating.

**Case Report**

Presented is the case of a 60-year-old man whom worked as a sandblaster for 25 years and generally did not use personal protective equipment in the workplace. Medical history is reported as active smoker, COPD, right upper lung pneumonia and tubercular esoohagocutaenous fistula.
During the months preceding hospitalization, the patient had suffered worsening dyspnea with no cough, fever, expectoration, or associated constitutional symptoms. Several randomly dispersed rhonchi were found in both lung fields upon auscultation. After observing laboratory tests, no significant findings were revealed. However, lung function testing showed a mixed pattern among forced vital capacity (FVC), forced expiratory volume (FEV) and forced expiratory flow. A diffuse bilateral nodular pattern with posterior opacities in the upper lung lobes was discovered on a chest x-ray. These opacities were associated with volume loss, retraction of the hila and compensatory emphysema of the lower lobes. In addition, bilateral hilar adenopathies with peripherally located egg-shell calcifications were also observed (See Figure 3 A,B,E,F). Upon examination of the thorax CT scan, opacities containing spotted pin-like calcifications were revealed. Paracatricial emphysema between the right upper lobe opacity and the adjacent pleura was also identified (See Figure 3 C and D).

These findings are consistent with PMF. The patient was advised to terminate smoking. Symptomatic treatment with bronchodilators and N-acetylcysteine was implemented. Upon discharge, the patient's respiratory situation was stable.

Treatments

Rapid deterioration of a patient presenting with pneumoconiosis disease may be due to several complications including massive fibrosis. PMF is an incurable disease. There is no established effective treatment regimen other than supportive care. Furthermore, few treatment options are available; most of these are focused on the management of symptoms brought on by the disease process. Bronchodilators, N-acetylcysteine, and corticosteroid therapy are available to potentially help manage the effects of the disease. In recent years, lung transplant has been an option for end-stage disease treatment. However, lung transplant is a difficult operation and organ donation is a barrier.

The best advice for those diagnosed with PMF is that those laborers participate in and are current on their preventative screening exams. Education and equipment, such as personal dust exposure monitors, which are not readily used for PMF and pneumoconiotic disease prevention should be utilized to their fullest. If PMF is diagnosed, it is suggested that the individual cease work in the industry immediately to prevent further, irreversible, damage.
Conclusion

Progressive Massive Fibrosis is a severely debilitating and fatal lung disease. Even without further dust exposure, those with the disease may exacerbate the condition at any given time. Amidst the enactment of regulatory measures and stable reporting, increasing prevalence of this potentially avoidable disease is confounding. Further study precaution, and enforcement must be explored and implemented. Overwhelming numbers of laborers take screening exams for granted; this causes missed opportunity for disease detection and possible prevention. In order to prevent future dust-induced illness and its associated death, industry and regulatory agencies must improve the effectiveness of workforce training, personnel protective equipment, and health protections.
References


Figure 2. Chest radiograph in a coal worker showing bilateral mass lesions (arrows) in the upper lungs with fibrotic change. The “angel’s wing” appearance suggests progressive massive fibrosis. Image Courtesy of: Yang JC, Liu KL. Coal workers’ pneumoconiosis with progressive massive fibrosis. CMAJ. 2012;184(16):E878-E878.