THE NORTHERN HOSPITAL

PULMONARY FIBROSIS

Josiah Wedgwood I (1730 -1795), portrait in Jasperware.

"May not Dr. Priestley's experiments of producing pure air be applied to the improving or changing of the air of sick rooms or hospitals?"

Commonplace Book of Josiah Wedgwood I, 1782.

In the early 1760s a small group of business men, scientists, writers, engineers, chemists and doctors formed themselves into a group that became know as the Lunar Society of Birmingham, so called because they would meet for dinner each full moon. In an age without street lighting and relative lawlessness, the full moon would provide the best and safest means by which members could make their way home in the early hours of the morning. This little group was drawn together by a common spirit of "enlightened" enquiry. They would discuss all manner of cutting edge scientific and humanistic issues into the small hours of the morning amidst much wine, food and entertainment. Amidst all the mirth and jocularity however, there was also a very serious side to these gatherings. Their discussions were not only for pleasure and camaraderie but were also aimed at the practical betterment of

mankind and society in general. If the so called "Industrial Revolution" can be said to have had its beginnings in mid Eighteenth century Birmingham, then it can be pinned even more precisely to the men of the Lunar Society. It was largely from this group that the future "captains if industry" of the Nineteenth century would model themselves. One needs only to look at the list of the names who made up the Lunar Society to appreciate the awesome impact it would have on subsequent world history, names that included Mathew Boulton, the iron and steel industrialist, William Withering, the discover of digoxin, James Watt, discoverer of the steam engine, Erasmus Darwin (grandfather of Charles), Joseph Priestly, discoverer of oxygen and not least of all Josiah Wedgwood I. Josiah was one of the original "captains of industry", starting out as potter of Burslem, expanding his trade to an unprecedented truly "industrial" extent and eventually becoming master potter to the Queen and the Empire.

By the late Seventeenth century Britain stood poised to dominate the world, there seemed to be no limit to what human industry, science and technology could achieve. However like most good things in life there would be a price to pay, even though this was not readily apparent to the men of the embryonic industrial revolution. That price, only really now truly apparent to those living in the early 21st century, would be the destruction of the environment and the realization of the consequences that this has had and will continue to have for the health of every living creature on the Earth.

Although Josiah and his Birmingham colleagues did not and could not have known the global consequences of what they helped set in motion, there were in fact early signs even in their day of what the future price of industry would entail. In Josiah's own factory he noticed ever increasing numbers of his potters coming down with an insidious "wasting" disease that primarily affected the lungs, resulting in severe respiratory incapacity and ending in premature retirement and an early death. He correctly surmised that "potters rot", as the disease became known, was due to atmospheric particles produced from grinding flint that was part of the pottery making process of the time. Unlike many of his contemporary industrialists however, he did actually care about the health of his workers. Upon reading an account of his good friend and fellow Lunar Society member, Joseph Priestley's discovery of "purified air" or oxygen as we now know it, he wondered whether or not this gas would be beneficial for his unfortunate workers who were suffering from potters rot. Another fellow Lunar Society member Dr Erasmus Darwin was convinced that it could and was prescribing "6 gallons of pure oxygene" per day to his consumptive patients.

The disease that Josiah's workers were contracting was silicosis, a particularly devastating form of pulmonary fibrosis. Whilst a big enough problem in Josiah's day it would be "small scale" compared with the devastating extent of the coal miner's pneumoconiosis that was to be the major cause of pulmonary fibrosis when the industrial revolution came into full fruition in the century that followed. In the 21st century we now reap the incredible benefits of the revolution that commenced with the men of the Birmingham Lunar Society, yet we also face the fierce challenges of its consequences to our health and the environment. Josiah Wedgwood was prescient in his thinking of "oxegene" as possibly beneficial to his workers. Whilst not a cure, as he had hoped, Dr Priestley's discovery is nonetheless an essential component of the treatment of pulmonary fibrosis in the 21st century. Unfortunately the captains of industry that followed Josiah have in the main been somewhat less concerned for the consequences of their industries.

PULMONARY FIBROSIS

Introduction

Pulmonary fibrosis is a general term describing a chronic and progressive pathophysiological process occurring in a range parenchymal lung diseases that result in a similar end point.

Terminology for this group of lung diseases varies. Other terms that essentially mean the same thing include:

- Diffuse interstitial lung disease.
- Interstitial pulmonary fibrosis.
- Cryptogenic fibrosing alveolitis (for idiopathic pulmonary fibrosis).

Pathophysiology

As a group, regardless of etiology, a common pathophysiology exists that begins with acute injury to the pulmonary parenchyma, leading to chronic interstitial inflammation, and ultimately progressing to the common end point of pulmonary fibrosis and tissue destruction.

The fibrous tissue reduces the distensibility of the lung just as a scar on the skin will reduce its distensibility. As a result the lung volumes are small and abnormally large pressures will be required to distend the lung.

The air ways are not specifically involved, and so airway resistance will be normal. Or in some cases even decreased because of the retractile forces exerted on the airway walls by the surrounding parenchyma are abnormally high.

Chronic hypoxia is due to diffusion impairment and ventilation-perfusion mismatch.

Causes

Pulmonary fibrosis can be idiopathic or secondary to a known group of aetiologies.

1. **Idiopathic,** (or cryptogenic fibrosing alveolitis).
    - The disease process is confined to the lungs.
    - Note that there are also a number of other distinct “variants” in the idiopathic category apart from “cryptogenic fibrosing alveolitis”. [3]
2. Sarcoidosis.
3. Environmental mineral dusts, (the pneumoconioses):

    The best documented causes include:

- Coal workers pneumoconiosis.
- Silicosis
- Asbestosis
- Berylliosis.

A range of other dust particles including steel, brass, lead, and pinewood have also been implicated with pulmonary fibrosis.

4. Radiation.

Less commonly:

5. Connective tissue/ Autoimmune:

   - Rheumatoid arthritis
   - Ankylosing spondylitis
   - Scleroderma

6. Infective

   - Tuberculosis.

7. Allergic alveolitis:

   This is due to an immunological reaction to inhaled organic material. Examples include:

   - Aspergillosis, (allergic bronchopulmonary)
   - Actinomycosis, ("Farmer's lung")
   - Alveolitis due to inhaled *avian proteins*, (in patients with close proximity to birds).

8. Drugs:

   Many have been implicated, the best documented include:

   - Amiodarone
   - Cytotoxic agents.

9. Toxins:

- Paraquat.

Complications

- Progressive respiratory failure.
- Right heart failure.
- Recurrent pneumonia.
- Pneumothorax.
- Increased risk of bronchogenic carcinoma.

Clinical Features

Most patients with idiopathic pulmonary fibrosis will be over 50 years of age.

The onset of symptoms is insidious.

The "classic" clinical features of pulmonary fibrosis include:

Symptoms:

1. Progressive shortness of breath
2. Dry cough is common.

Signs:

1. Cyanosis is common in later stages.
2. Clubbing:
    - This is seen in up to 50% idiopathic cases.
3. Chest auscultation:
    - Fine (*"velcro" like*) inspiratory crepitations, especially at the end of inspiration.
4. Chest expansion reduced.
5. Respiratory pattern typically is rapid breathes (tachypnea) and shallow breathes (smaller tidal volumes). This pattern will minimize the work of breathing with restrictive lung disease, (in comparison with airflow obstruction where the breathing pattern tends to one of relatively slower breaths with greater tidal volumes).

Clinical Assessment on ED Presentation

Important points of history include:

1. Establish history of the presenting complaint.

2. Establish whether a definite diagnosis of pulmonary fibrosis has been made.

3. Establish the patient's normal level of function and quality of life.

4. Is the patient on home oxygen?

5. If the patient's disease is end stage, establish whether or not there is any **Advanced Care Plan** in place.

Important points of examination

1. Immediate assessment of oxygenation, pulse oximetry

2. Look for fever, especially evidence of chest infection.

    - The majority of patients with pulmonary fibrosis who present to the ED will do so because of chest infection.

Investigations Making the Diagnosis

Note that in addition to investigations a thorough history for the known aetiologies for pulmonary fibrosis is also an essential part of the establishment of a diagnosis.

ABGs

Typical blood gas analysis will show the following:

- PaO_2 is low. This is due to impaired oxygenation.

- $PaCO_2$ is low. This is probably due to mild hyperventilation due to chronic hypoxia.

- pH is usually normal unless there is an acute exacerbation of disease.

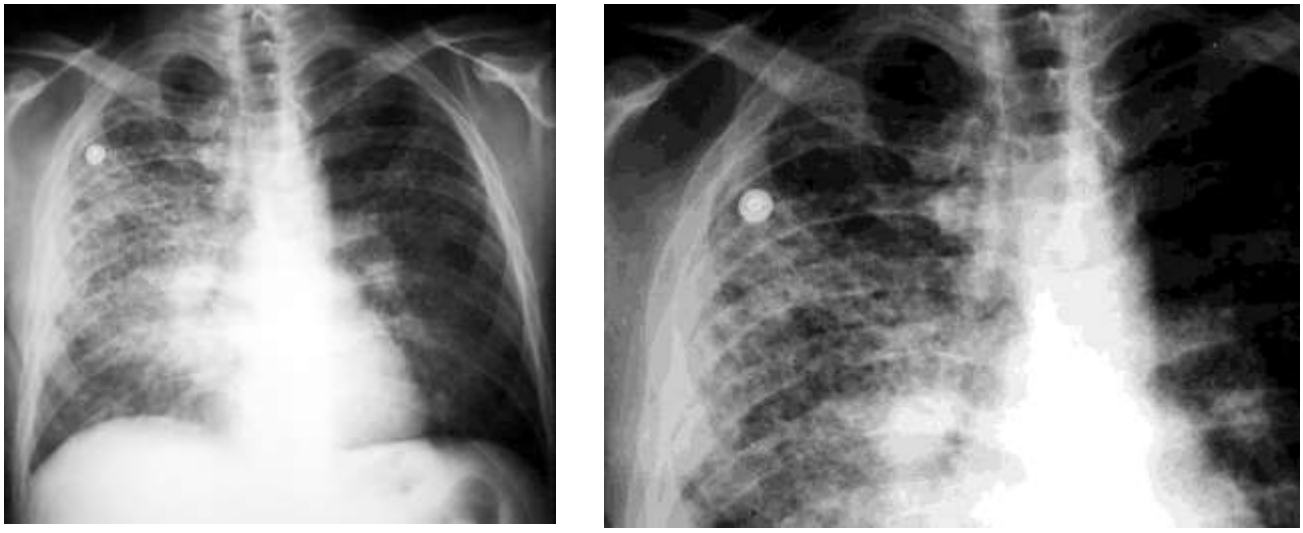
CXR

Typical chest x-ray changes may include the following: [2]

- In early disease the CXR may appear normal.

- With advancing disease lung volumes are reduced with elevated hemi-diaphragms and decreased rib spacings.

- Bilateral pulmonary reticular infiltrates.
- Small nodules may be seen or a combination “reticulo-nodular” pattern
- There may be a generalized “ground glass” attenuation of the lung fields. This may be described as a generalized haziness of the lungs, as if a veil had been drawn across the radiograph.
- In more advanced disease “honeycombing” may be seen. This term applies to end stage fibrosis where multiple cystic or “honeycomb” like spaces can be seen.



Honeycombing appearance of end stage pulmonary fibrosis.

- When compared to previous x-rays these changes can be seen to be chronic in nature.
- The location of the fibrotic changes within the lung fields may suggest the pathology:

Upper lung field fibrotic changes will be predominantly caused by:

S Silicosis, sarcoidosis

C Coal worker’s pneumoconiosis.

A Ankylosing spondylitis, allergic alveolitis.

T Tuberculosis

O Other, radiation, drugs.

Lower lung field fibrotic changes will be predominantly caused by:

R Rheumatoid arthritis.

A Asbestosis.

S Scleroderma

I Idiopathic

O Other, radiation, drugs.

Occasionally more disease specific changes may be seen, such as asbestos pleural plaques that are seen in cases of asbestosis.

High Resolution CT Scan

- This is very useful for the diagnosis of pulmonary fibrosis. It is much more sensitive than plain x-ray.
- It is also useful for establishing the extent and progression of disease.

Lung Function Tests

Spirometry [1]

1. This shows a restrictive pattern of disease.
    - The FEV_1 is reduced.
    - The FVC is markedly reduced.
    - The FEV_1 / FVC *ratio* may be normal or higher than normal.
2. Lung volumes:
    - All lung volumes are reduced including, TLC, FRC and RV although the relative volumes are preserved.

Diffusion tests

- The DLCO transfer factor will be reduced.

Airway resistance and reversibility

- Airway resistance is not seen in uncomplicated cases of fibrosis.

Lung Biopsy:

- This (thoracoscopic or open) may ultimately be required to make a histological diagnosis of pulmonary fibrosis.

Investigations

In acutely unwell patients who present to the ED in respiratory distress, the following investigations will need to be considered:

1. Bloods:
    - FBE.
    - CRP.
    - U&Es / glucose.
    - ABGs, (as indicated).
    - Blood cultures, (as indicated)
    - Others as clinically indicated.
2. CXR

    In particular looking for:
    - Infection / consolidation
    - Pneumothorax.
    - Progression of known disease.
    - New disease, such as malignancy or effusions.
3. ECG
    - Routine as for any unwell dyspneic patient.

Management

Issues will include:

1. Oxygenation.
2. Treatment of any infection.
3. Establishing the patient's normal level of function and deciding on whether NFR issues are appropriate.
4. Role of steroids/ cytotoxic agents.

Oxygenation

- **This is the priority as for any acutely unwell and hypoxic respiratory patient.**
- In pure fibrosis, carbon dioxide retention is not a feature. If present it indicates patient exhaustion or frank respiratory failure.
- The role of *non-invasive ventilation* is less well established for patients with pulmonary fibrosis than is the case with COPD/ asthma, but is worth trying ahead of intubation.
- It is especially useful for delivery of 100% oxygen or cases of co-existing pathology such as CCF/ COPD and as a possible means of avoiding intubation.
- The decision to intubate will depend on the usual factors influencing this decision in any patient with chronic lung disease.

Treat any infection.

- Most presentations to the ED in patients who have pulmonary fibrosis will be for pneumonia.
- Besides oxygenation this will be the most important treatment.

Establish normal level of function and decide on whether NFR issues are appropriate

- Many patients with fibrotic lung disease will be "end stage", and so it will be important to try to establish early how far treatment interventions should appropriately be taken in order to design an ED management plan.
- Ideally these issues should be sorted before patients attend the ED acutely unwell, however often they will not have been, making ED management more problematic in the very unwell patient.

Role of steroids/ cytotoxic agents [3]

- Steroids are usually used in idiopathic cases in an attempt to stop or slow inflammatory changes becoming those of end stage fibrosis.
- Steroids should be initiated *early* in the disease process in the hope that the progression to irreversible fibrosis can be delayed for as long as possible
- The response to steroids in any given case, however is variable and overall is generally poor.
- Cytotoxic agents such as cyclophosphamide and azathioprine are sometimes used by Respiratory physicians.

Transplant

- Lung transplant may ultimately be suitable for a small number of patients.

Prognosis

- This will depend largely on the cause.
- The rate of progression is variable depending on the cause and can range from slow and insidious over a period of years to rapidly progressive over several months.
- Once fibrosis occurs the pathological change is not reversible.
- **Idiopathic** cases generally carry the worst prognosis, the disease progress being relentless and irreversible with death occurring approximately 2 years after diagnosis. [3]

References

1. West JB, Pulmonary Pathophysiology, 5th ed. 77-93.
2. Rosen P et al, Diagnostic Radiology in Emergency Medicine, 1992, p. 292.
3. Respiratory Therapeutic Guidelines 3rd ed 2005.

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