DIFFUSE PANBRONCHIOLITIS: A MIMICKER OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Summary

We report a 69-year-old patient presenting with chronic productive cough, progressive dyspnoea, airflow obstruction and respiratory failure. He was mislabeled as having chronic obstructive pulmonary disease (COPD) in the past. Review of his clinical and radiological features finally led to a diagnosis of diffuse panbronchiolitis (DPB). He responded dramatically to long-term low dose erythromycin. The clinical, radiological and pathological features of the condition are reviewed. It is important not to miss the diagnosis of DPB as it is a potentially treatable condition.

Introduction

Diffuse panbronchiolitis (DPB) is a distinct clinico-pathological entity characterized by chronic sinusitis and bronchial inflammation. The symptomatology of DPB bears similarities with chronic obstructive pulmonary disease (COPD) and bronchiectasis. We report an elderly patient with DPB, being mislabeled initially as COPD. As COPD is a common disorder in the elderly, a high index of suspicion is needed to differentiate DPB from COPD. It is important to make this distinction, as DPB is a potentially treatable disease when discovered early.

Case Report

A 69-year-old man was admitted to our department because of dyspnoea and cough with purulent sputum in December 1996. He worked in the construction site in the past and gave a 22 pack-year smoking history. He had complained of progressive shortness of breath, frequent cough with purulent sputum for three years. He also reported chronic nasal congestion and discharge. His exercise tolerance was reduced to a few steps on level ground and he was home bound, requiring assistance in his activities of daily living. Positive physical findings included diffuse wheezes and crackles over the chest. He sought treatment in various places before seeing us and had been labeled as having COPD, chronic bronchitis and congestive heart failure in the past, and treated as such without improvement.

Initial investigations showed a normal blood picture and differential counts, biochemistry, renal and liver profiles. Chest radiographs showed diffuse micronodules of 2 to 3 mm diameter mainly located in the lower zones. Electrocardiogram was normal. Arterial blood gases showed type 2 respiratory failure with PaO2 of 8.1 kPa (SaO2 91%) and PaCO2 of 7.2 kPa. Sputum grew a mixed growth of Streptococcus pneumoniae and Haemophilus influenzae, and was negative for Mycobacterium tuberculosis and malignant cells. Transthoracic echocardiogram showed satisfactory left ventricular function with normal heart valves. A definitive diagnosis was not made and he was treated symptomatically with bronchodilator, a course of appropriate antibiotics and systemic corticosteroid. Pulmonary function test, high resolution computed tomography (HRCT) of the thorax and computed tomography (CT) of the paranasal sinuses were arranged.

Pulmonary function tests when he was stable revealed severe airflow obstruction, hyperinflation, air trapping, maldistribution of ventilation and reduction in gas transfer: the forced expiratory volume in one second (FEV1) was 0.86L (52% predicted), forced vital capacity (FVC) 1.28L (61% predicted), FEV1/FVC of 67%, total lung capacity (TLC) by whole body plethysmograph was 5.13L (116% predicted), residual volume (RV) 3.81L (234% predicted), RV/TLC was 74%, alveolar volume by single breath helium dilution was 2.20L (50% predicted).
predicted) and diffusing capacity for carbon monoxide (DLCO) was 41% predicted.

CT of paranasal sinuses showed diffuse polyposis and mucosal thickening. High resolution computed tomography of thorax (Figure 1) showed air trapping and diffuse bronchiectatic changes. The most remarkable feature was the presence of numerous branching subpleural centri-lobular nodules especially in the lower zones, resembling tree-in-bud. His cold agglutinin was subsequently found to be raised at a titre of 1:512, with anti-I specificity. Antibodies for mycoplasma, chlamydia and legionella were negative.

The overall picture was consistent with the diagnosis of diffuse panbronchiolitis. An open lung biopsy was planned but the patient deteriorated significantly in June 1997 with a bout of severe infective exacerbation with Haemophilus influenzae and Moraxella catarrhalis. His blood gases showed PaO2 of 5.2 kPa (SaO2 75%) and PaCO2 of 6.8 kPa on room air. He was treated with appropriate antibiotics, bronchodilators and corticosteroid. His condition stabilized with a PaO2 of 7.9 kPa (SaO2 91%) and PaCO2 of 6.9 kPa on discharge. He declined open lung biopsy after considering the possible risks, but agreed to a bronchoscopy. No abnormality was detected on bronchoscopy and a transbronchial biopsy only revealed non-specific inflammation.

Because of the consistent clinico-radiological picture and deterioration with symptomatic treatment, empirical low dose erythromycin was started at a dose of 250mg twice daily in July 1997. He reported marked symptomatic improvement at the review in October 1997, with an exercise tolerance of 100 metres on level ground and an SaO2 of 93% on room air (resting). He was able to leave home on his own and resumed independence in his daily living. FEV1 improved to 1.05L (70% predicted), FVC 1.59L (82% predicted) in October 1997, and FEV1 further improved to 1.27L (87% predicted) and FVC to 1.88L (102% predicted) in May 1998. He is now maintained on long term low dose erythromycin and inhaled bronchodilator.

Discussion

Diffuse panbronchiolitis (DPB) is a distinct clinico-pathological entity characterized by chronic sinusitis and bronchial inflammation1. It usually occurs in the second to fifth decade and two-thirds of patients are non-smoker. It was first described in Japan and most reported cases were in Japan2, and in other Asian countries like Korea3. Sporadic cases have been reported in non-Asian countries4, 5,6. Tsang et al recently reported seven Chinese cases with a mean age of 487. It is a disease of unknown aetiology characterized by progressive airflow limitation, chronic paranasal sinusitis and lower airway infection. Inflammation of the respiratory bronchioles with accumulation of lipid-laden ‘foamy’ macrophages is a characteristic, though not diagnostic pathological finding8.

Clinical diagnostic criteria include the followings2: (1) chronic cough with sputum and exertional dyspnoea; (2) physical signs of coarse crackles and rhonchi; (3) chest radiograph showing disseminated fine nodular shadows, mainly in the lower lung fields, with hyperinflation of the lungs; and (4) pulmonary function tests showing at least three of the following abnormalities: (i) FEV1 less than 70% predicted; (ii) FVC less than 80% predicted; (iii) RV greater than 150% predicted and (iv) PaO2 less than 10.6 kPa. Chronic parasinusitis is present in almost all patients with DPB and most patients have elevated cold agglutinin titres (1:512 to 1:2048) with anti-I specificity1. Japanese patients have a high prevalence of HLA-Bw548. Sputum often grows Streptococcus pneumoniae and Haemophilus influenzae in the early stage, and Pseudomonas aeruginosa in more advanced disease1.

Radiologically DPB is characterized by hyperinflated lung with tram-line or ring shadows of bronchiectatic changes. Diffuse, ill-defined micronodules of about 3mm diameter are present in the lung fields, mainly in the lower zones. On high resolution CT these nodules are distributed in a centri-lobular fashion and are frequently seen to be connected to linear, branching structures10. This is sometimes referred to as a tree-in-bud appearance and represents inflammation around
the respiratory bronchioles, bronchiolectasis and mucus plugging. Pathologically the most peculiar feature is the presence of dense aggregates of foamy histiocytes in the interstitium, especially in and around the walls of respiratory bronchioles (Figure 2)\(^8,10\), and this is referred as the “unit” lesion.

Low dose erythromycin (200 to 600 mg/day) and other macrolides has been shown to be effective in the treatment of DPB\(^11,12\), with improvement in dyspnoea, pulmonary function, radiographic appearance and blood gases. The mechanism of action is not known, but it is widely held that it is not due to direct anti-bacterial action, as the serum and sputum erythromycin levels are below the minimal inhibitory concentrations of common infecting organisms at the dosage used\(^12\). Proposed mechanisms of actions of macrolides include inhibition of elastase production by Pseudomonas aeruginosa\(^13\), reduction of sputum production\(^14\), inhibition of microvascular leak\(^15\), reduction of neutrophil chemotactic activity\(^16\), and attenuation of the up-regulation of neutrophil adhesion molecule Mac-1 in DPB\(^17\).

It is recommended that treatment should be tried for at least 2 months, and be continued indefinitely if no side effect develops\(^18\). Erythromycin (400 to 600 mg/day), clarithromycin (200 to 400 mg/day) or roxithromycin (150 to 300 mg/day) can be used. Clinical symptoms, chest imaging, pulmonary function and blood gases should be followed up.

Our patient has all the features of DPB including chronic productive cough, dyspnoea, chronic paranasal sinusitis, raised cold agglutinin titre, typical radiological features and pulmonary function findings. However, because of the similarities in the symptomatology of DPB and COPD, chronic bronchitis and various forms of bronchiectasis, the diagnosis was made with considerable delay in this patient. He is also older than the mean age of the reported Chinese series\(^7\). The clue to diagnosis was the chest radiographic appearance, which was not typical of the usual COPD or emphysema. HRCT thorax lent further support to the diagnosis. Although an open lung biopsy was not possible in this patient, he responded dramatically to low dose erythromycin.

As COPD is a common disease in the elderly, it is all too easy to label an elderly patient with chronic cough, sputum production, dyspnoea, airflow obstruction, and respiratory failure as having COPD or bronchiectasis, especially if he or she has smoked. This case illustrates the need to maintain a high index of suspicion and to consider DPB a potential differential diagnosis. Failure to make a specific diagnosis of DPB may deny the patient a chance to recovery.

References
A fatalistic “it is old age...nothing more can be done” attitude has been quite prevalent among doctors when confronted by the conditions encountered in elderly patients. These problems are often complex and they span over a person-space-time dimension of a whole person (not just her parts) interacting with her environment (physical as well as psychosocial) over a period of time (not just a single moment). Because of their complexity, these problems are seldom susceptible to a simple solution, and are often frustrating to those tuned to singular presentations capable of single diagnosis and simple solution.

The growth of knowledge base in Geriatric Medicine now permits choice and the “chosen” elderly patient can improve functionally in most cases. Setting aside the question of whether an elderly person can choose or not, there remains the disturbing question of what is the Choice of the society in general and of the medical profession in particular.

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“MATTERS OF FATE HAVE BECOME MATTERS OF CHOICE”

JUSTICE MARIE GARIBALDI, NEW JERSEY 1987