

CASE REPORTS

streptococcal necrotizing fasciitis. Aggressive and extensive surgical debridement or amputation to remove the necrotic tissue are also indicated. Vancomycin has been successfully used in some cases of severe and life-threatening streptococcal infection in which penicillin treatment had failed³. In this particular case, no antibiotics was given even though he sustained a grade I compound fracture. Whether this would have prevented the necrotizing fasciitis is debatable. Nevertheless, the antibiotic regimens currently recommended by Ministry of Health for this purpose would have covered for group A Streptococcus.

Intravenous immunoglobulin may also have a role in the management of such cases. It can reverse the hyperproliferation of T cells, neutralise superantigens and regulate the production of tumour necrosis factor³.

Acknowledgement

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References

1. Francis KR, Lamaute HR, Davis JM, Pizzi WF. Implications of risk factors in necrotizing fasciitis. *Am J Surg* 1993;59(5) : 304-8.
2. Stevens DL. Invasive group A Streptococcus infections. *Clin Infect Dis* 1992;14 : 2-13.
3. Yong JM. Necrotizing fasciitis (letter). *Lancet* 1994;343(4) : 1427.

A Report of the First Three Cases of Diffuse Panbronchiolitis in Malaysia

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Summary

Three cases of diffuse panbronchiolitis (DPB) occurring in two Malaysian Chinese patients and one Malay patient are reported. They had similar clinical, radiological and physiological features which are characteristic of DPB. The diagnosis in one of the cases was confirmed histologically by transbronchial lung biopsy. These could be the first three cases identified in Malaysia.

Key Words: Diffuse panbronchiolitis, Malaysians

Introduction

Diffuse panbronchiolitis (DPB) is a disease first described in Japan which is rare in the West but not uncommon amongst Orientals¹. It is characterized by small airway obstruction due to inflammation of the terminal and respiratory bronchioles. Its aetiology remains unknown. Although clinically it may mimic bronchiectasis, the radiographic appearances in DPB are characteristic. We report here three cases of diffuse panbronchiolitis believed to be the first three cases identified in Malaysia.

Case Reports

Case 1

A twenty-nine-year-old Malaysian Chinese housewife was seen in our respiratory clinic for chronic cough since the age of sixteen years. The cough was associated with marked expectoration of yellowish-green sputum and occasional wheeze. No history of whooping cough, measles, pulmonary tuberculosis or recurrent chest infections in childhood was elicited. Although she could still cycle short distances, over the past year she had become increasingly breathless on exertion. She had never smoked and there was no family history of similar illness.

Physical examination revealed a slightly built young woman. The blood pressure was 100/60 mmHg, pulse rate was 84/minute and respiratory rate of 16/minute. There was no pallor, cyanosis or oedema but finger clubbing was present. On auscultation coarse crackles with expiratory wheeze were heard over the mid and lower zones of both lung fields. The rest of the examination was unremarkable. Lung function tests showed a marked obstructive picture with forced expiratory volume at one second (FEV_1) 0.6 litre (23% predicted), forced vital capacity (FVC) 1.1 litre (34% predicted), FEV_1/FVC ratio 54% and peak expiratory flow rate (PEF) 160 l/minute (35% predicted).

Her chest radiograph showed generalized overinflation, multiple nodules in both lung fields and bronchiectatic changes especially in the mid and lower zones (Fig. 1). Sputum culture yielded no growth.

High resolution computerized tomography (HRCT) of

the thorax confirmed bronchiectasis of varying degrees involving both lungs with scattered nodules. These changes and the clinical presentation were thought to be consistent with diffuse panbronchiolitis (DPB). The patient subsequently underwent diagnostic bronchoscopy which showed increased amounts of sputum within all the bronchi with diffusely inflamed mucosa. A transbronchial lung biopsy performed from the right middle lobe showed bronchiolar tissue with a dense peribronchiolar infiltrate of mainly lymphocytes, plasma cells and macrophages. Scattered neutrophils were seen within the bronchiolar epithelium. These features support the diagnosis of DPB. The patient was treated with bronchodilators and mucolytics and later with steroids (prednisolone 40 mg daily for two weeks) but showed only minimal response. She was subsequently commenced on erythromycin 500 mg daily with slight subjective improvement after three months although spirometry remained unchanged.

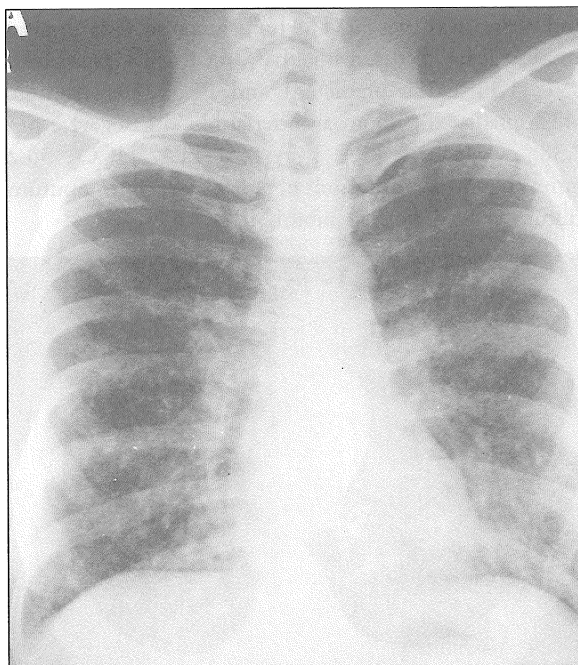


Fig. 1: Chest radiograph of patient 1 showing generalized hyperinflation, multiple nodules in both lung fields and bronchiectatic changes especially in the mid and lower zones

Case 2

A forty-two-year-old Malaysian Chinese male was referred from another hospital with a ten-year history of cough with purulent greenish sputum and a two-year history of progressive exertional dyspnoea associated with ankle swelling for which he had been on intermittent treatment from his general practitioner. His effort tolerance had deteriorated over this period to such an extent that he was confined to his house. At the age of eleven years he had undergone a nasal operation for recurrent nasal discharge but had no symptom of sinusitis at the time of examination. He was a non-smoker and did not keep pet. He worked as a film projectionist. Physical examination revealed a tachypnoeic young man not cyanotic but had clubbing of the fingers. His pulse rate was 80/minute, blood pressure was 120/80 mmHg and respiratory rate of 24/minute. Bilateral oedema of the lower extremities was present up to the knees and his jugular venous pressure was elevated. Coarse crackles were heard over both lung fields particularly in the lower zones. The liver was palpable six centimetres below the right costal margin and ascites was present. His lung function tests showed an obstructive picture with FEV₁ 0.61 (20% predicted), FVC 1.11 (31% predicted) and PEF 250 l/minute (42% predicted). Room air arterial blood gases were pH 7.38, pCO₂ 6.94 kPa, pO₂ 8.51 kPa, HCO₃ 30.2 mmol/l and a saturation of 91.9 per cent. Sputum culture yielded normal mouth flora.

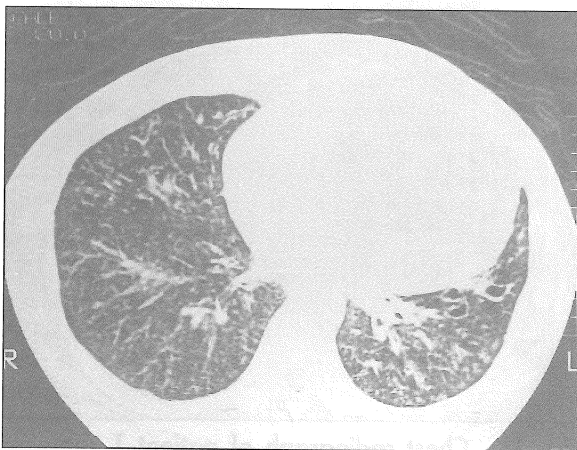


Fig. 2: HRCT of the thorax of patient 2 showing bronchiectasis of varying degrees involving both lungs with scattered nodules

His chest radiograph showed minimal hyperinflation, cardiomegaly and bronchiectasis in parts of the lung fields. Echocardiography showed good left ventricular function with an ejection fraction of fifty three per cent, gross dilatation of the right ventricle and right atrium, and moderate tricuspid regurgitation. The main pulmonary artery was dilated. HRCT showed bronchiectasis of varying degrees involving both lungs with scattered nodules (Fig. 2). The clinical, physiological and radiological findings were consistent with those found in DPB.

The patient was commenced on erythromycin 500 mg daily, diuretic, and inhaled ipratropium bromide and salbutamol. The erythromycin was intended to be continued for three to six months. The patient however failed to return for follow up.

Case 3

A thirty-seven-year-old Malay man, a hostel caretaker presented for the first time to the respiratory unit in 1987 with a week history of dyspnoea associated with wheezing, greenish sputum and low grade pyrexia. There was no symptom to suggest pulmonary tuberculosis.

In his childhood he was diagnosed to have bronchial asthma when he presented at the age of six with dyspnoea and wheezing. He claimed that his father and younger brother were asthmatic too. His asthma was stable as he only had infrequent exacerbations, requiring outpatient treatment with oral theophylline and salbutamol from another hospital and several private clinics. He also suffered from chronic paranasal sinusitis. He was a light cigarette smoker as he smoked only ten cigarettes per day for two years only.

Clinical examination upon his first presentation revealed a thin man who was dyspnoeic at rest but not cyanosed. He was febrile with a temperature of 38 degree Celsius. There was no clubbing of the fingers or ankle oedema. He was barrel-chested with reduced chest expansion bilaterally. Widespread rhonchi and bilateral mid zone and basal coarse crackles were heard on auscultation.

Arterial blood gases on breathing room air showed pH 7.35, pCO₂ 4.4 kPa, pO₂ 8.35 kPa, HCO₃ 20.1

mmol/l and a saturation of 92%. Pulmonary function testing was consistent with severe obstructive ventilatory defect with FEV₁, 1.1l (30% predicted), FVC 3.21 (24% predicted), FEV₁/FVC ratio 42% and PEF 90 l/min (25% predicted). His chest radiograph showed generalized overinflation, multiple nodules at the mid and lower zones and bronchiectatic changes of the proximal and peripheral bronchi. Sputum for culture yielded no growth. HRCT of the thorax demonstrated disseminated small nodules in both lungs with bronchiectatic changes affecting mainly small bronchioles. Based on the typical clinical presentation, the progress of the disease despite adequate therapy and classical radiological features, the diagnosis of DPB was made. The patient was treated with inhaled bronchodilators and steroids and later subjected to a trial of ofloxacin 500 mg daily. The ofloxacin was intended to be continued for six months and further progress is awaited.

Discussion

DPB is a disease characterized by chronic inflammation located mainly in the region of the respiratory bronchioles. Its aetiology remains unknown. It was first described in Japan in 1969 by Yamanaka and co-workers¹ and is recognized as a separate entity from bronchial asthma, chronic bronchitis, pulmonary emphysema, bronchiectasis and alveolitis. It is prevalent in Japan, China and Korea but rare in America and Europe. We believe that our report is the first of this condition seen in Malaysians. Two of them are ethnically Chinese but Malaysian born. This lends support to the view that the disease is more common in Orientals, and that there may be genetic predisposition rather than environmental factors. The third case occurs in a Malay man. The clinical features of chronic cough, with sputum production and dyspnoea, together with radiological changes of diffuse fine nodular changes, more prominent in the lower lung fields, and physiological changes of obstructive defect on lung function testing are characteristics of DPB which were present in all the three cases. Because of the patient's poor clinical condition, transbronchial lung biopsy could only be performed in Case 1, and the procedure confirmed the diagnosis of DPB. Case

2 and 3 had all the clinical, radiological and physiological features of DPB and their HRCT in particular were typical of DPB as described by Akira *et al*². The presence of both small nodules and dilatation of small airways is consistent with type III HRCT classification as proposed by Akira *et al*. This HRCT classification is useful for assessment of severity of the disease and corresponds to clinical and histopathological severity. The basic histopathological lesion is a mononuclear infiltration of the respiratory and terminal bronchioles with infiltration by lymphocytes, plasma cells and histiocytes and extension of these inflammatory changes towards the peribronchiolar area. Most of these changes are seen in the transbronchial biopsy of Case 1.

Treatment of diffuse panbronchiolitis has largely been supportive. Bronchodilators, steroids and antibiotics for suspected or proven chest infection have been used. The role and efficacy of steroids is uncertain and even questionable. Recently "low dose, long term" erythromycin therapy has been reported to be effective in DPB³. Erythromycin in a daily dose of 400-600 mg daily for at least 2 months resulted in clinical improvement which was accompanied by radiological improvement. The mechanism of action of erythromycin in DPB is however uncertain. It is currently the focus of intensive research in Japan. Case 1 and 2 are presently being treated with this drug. Case 3 is presently on ofloxacin which has also been reported to be beneficial. The overall prognosis appears to be better if it occurs in young patients below the age of forty and if there is no chronic superinfection by *Pseudomonas aeruginosa*. The detection of these three cases makes us believe that DPB is probably more common than previously thought and many cases may have been misdiagnosed as bronchiectasis or chronic bronchitis. We are now on the lookout for more cases especially to see if DPB also affects Malaysians of Indian descent.

Acknowledgement

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References

1. Yamanaka A, Saeki S, Tamura S, Saito K. The problems of chronic obstructive pulmonary disease: especially concerning about diffuse panbronchiolitis. *Intern Med* 1969;23 : 442-51.
2. Akira M, Kitatani F, Lee YS, *et al.* Diffuse panbronchiolitis: Evaluation with high resolution CT. *Radiology* 1988;168 : 433-8.
3. Nagai H, Shishido H, Yoneda R, Yagamuchi E, Tamura A, Kurashima A. Long term low dose administration of erythromycin to patients with diffuse panbronchiolitis. *Respiration* 1991;58 : 145-9.

Glibenclamide Induced Chronic Cholestasis Simulating Primary Biliary Cirrhosis : A Case Report

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Summary

A 43-year-old lady with long standing non-insulin dependent diabetes mellitus on glibenclamide presented with cholestatic liver disease. Initially she was thought to have developed primary biliary cirrhosis (PBC). When she made a spontaneous recovery following the withdrawal of glibenclamide, it became obvious that the patient had been suffering from drug-induced chronic cholestasis (DICC). The subtle differences between PBC and DICC are highlighted.

Key Words: Vanishing bile duct syndrome, Drug-induced chronic cholestasis, Pseudo-primary biliary cirrhosis sulphonylureas

Introduction

Glibenclamide is commonly used in the treatment of non-insulin dependent diabetes mellitus (NIDDM). Its well known side effects are rash and hypoglycaemia. We describe a patient in whom the sulphonylurea caused chronic cholestasis mimicking primary biliary cirrhosis.

Case Report

A 43-year-old Chinese lady was diagnosed as non-

insulin dependent diabetes mellitus (NIDDM) since 1986 and was controlled with glibenclamide 10 mg twice a day. She was well till September 1991 when she was admitted to the hospital with a four-day history of generalised itching and yellow discoloration of eyes.

Physical examination revealed a markedly jaundiced patient with excoriation marks all over her body. The