Case Report

Diffuse Panbronchiolitis: Report of a Rare Disease from India

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ABSTRACT

Initially described by a group of Japanese clinicians and pulmonary pathologists to distinguish it from other chronic obstructive lung diseases, diffuse panbronchiolitis (DPB) is an uncommon disorder which has been reported largely from the eastern world. It is imperative to recognise this condition because of its potentially treatable nature. Recently, long-term macrolide therapy has revolutionised its management. Herein, we describe a 65-year-old male who was being managed as a case of chronic bronchitis before this diagnosis was suspected and proved. **[Indian J Chest Dis Allied Sci 2009;52:43-45]**

Key words: Diffuse panbronchiolitis, Lungs, Bronchiectasis.

INTRODUCTION

Diffuse panbronchiolitis (DPB), now a well recognised entity, was described in the early 1960s by a group of Japanese clinicians and lung pathologists.[1] The term DPB was coined by Yamanaka and colleagues in 1969 to distinguish it from chronic bronchitis and the international scientific community became aware of this new entity in early 1980s.[2] ''Diffuse'' refers to the distribution of the lesions throughout both lungs, and ''pan'' refers to the involvement of inflammation in all layers of the respiratory bronchioles. The diagnostic criteria for diagnosis of DPB was laid down by the Ministry of Health and Welfare of Japan in 1998[3] which is: *(i)* persistent cough, sputum and exertional dyspnoea; *(ii)* past history of or current chronic sinusitis; *(iii)* bilateral diffuse small nodular shadows on a plain chest radiograph or centrilobular nodular shadows on chest CT images; *(iv)* coarse crackles; *(v)* FEV_1 / FVC less than 70% and PaO_2 less than 80mmHg, and *(vi)* titres of cold haemagglutinin equal to or higher than 64. A definite diagnosis of DPB can be made if the subject fulfils the first three criteria, and at least two of the last three criteria. If considered separately, these criteria[3] are non-specific and can lead to a misdiagnosis, such as chronic bronchitis, and therefore, to an inadequate treatment.

Diffuse panbronchiolitis has been described from various parts of the globe but a proven case of DPB has not been reported from the Indian subcontinent, to the best of our knowledge.

CASE REPORT

A 65-year-old non-smoker male presented to our out-patient service with one year history of cough with copious mucopurulent expectoration. He also had past history of recurrent sinusitis. His previous medications included oral theophylline (150mg twice daily) and inhaled corticosteroids (beclomethasone 200 µg twice daily). He had no significant improvement in his symptoms with these medications and over last six months he had rapid worsening of symptoms. He also developed breathlessness (Medical Research Council, grade IV) within this duration. His general physical examination revealed tachycardia, tachypnoea and grade III clubbing. Respiratory system examination showed no clinical feature suggestive of hyperinflation and on auscultation coarse crackles were heard in both the lung fields.

Chest radiograph showed bilateral reticulonodular opacities with lower lobe predominance. Pulmonary function tests revealed a vital capacity (VC) of 2,100mL (79.5% of the predicted value), forced expiratory volume in the first second (FEV_1) of 1,810mL (76.3% of the predicted value) and residual volume (RV) of 1,780mL (142.7% of the predicted value). Total lung capacity and diffusing capacity were not performed.

Arterial blood gases showed mild respiratory alkalosis and moderate hypoxaemia on room air.Microbiological profile was non contributory to the diagnosis. High-resolution computed tomography (HRCT) showed diffuse bronchiectatic changes involving all areas but lower lobes were predominantly involved and multiple centrilobular nodules with “tree in bud” appearance (Figure 1A). Areas of mosaic attenuation were also seen. Dynamic computed tomography (CT) confirmed these areas to be consistent with air trapping.

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Laboratory tests revealed an elevated erythrocyte sedimentation rate of 60mm at the end of the first hour, a C-reactive protein level of 7.6mg / dL, a white blood cell (WBC) counts of 6,000 / µL and haemoglobin level of 9.4mg / dL. Biochemical parameters were within normal limits except mild hypoalbuminemia (3.5mg / dL). The antinuclear antibodies were positive (2+; speckled pattern), however, double stranded deoxyribonucleic acid (dsDNA) was negative. Serology for rheumatoid

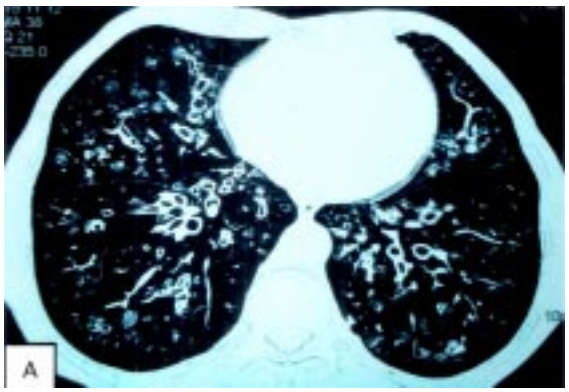

Figure 1A. HRCT chest showing diffuse bronchiectasis and centrilobular nodules involving lower lobes.

factor and human immunodeficiency virus (HIV) were negative. *Mycoplasma* serology and cold agglutinins were negative. He was also worked up for allergic bronchopulmonary aspergillosis; however, skin test for *Aspergillus* hypersensitivity was negative and total immunoglobulin E (IgE) and *Aspergillus* specific IgE levels were within normal limits. Alpha-1-antitrypsin levels and sweat chloride levels were also within normal limits. Human leukocyte antigen (HLA) serotyping was not performed.

Overall features were suggestive of small airway disease and the patient fulfilled the clinical criteria for the diagnosis of DPB laid by the Ministry of Health and Welfare of Japan.[3] Confirmation of diagnosis was achieved by surgical lung biopsy which showed a bronchiolocentric pattern of inflammation. There was transmural and peribronchial infiltration by lymphocytes, plasma cells and histocytes and prominent involvement of respiratory bronchioles which was consistent with DPB (Figure 1B). He was started on erythromycin 250mg QID, inhaled bronchodilators and high protein diet.

After three months of follow-up, the patient had significant decrease in sputum quantity and dyspnoea. On follow-up we learned that he has suffered from right-sided hemiparesis. A non contrast computed tomography (CT) of the head was obtained which was suggestive of right middle cerebral artery infarct. He was started on antiplatelet and antiepileptic treatment

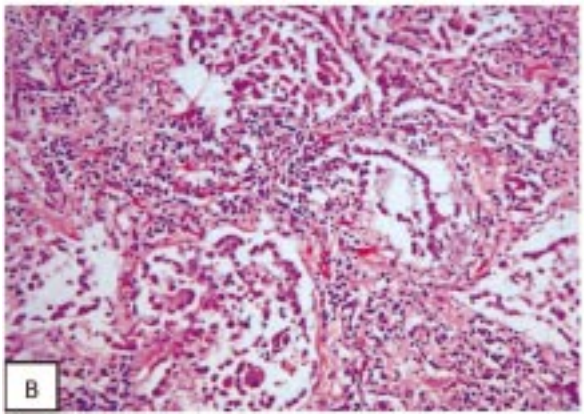

Figure 1B. Photomicrograph showing peribronchial infiltration by lymphocytes, plasma cells and histocytes and prominent involvement of respiratory bronchioles.

under Neurology Department from our institute. Subsequent information about his status is not known as the patient did not turn up for further follow-up.

DISCUSSION

Majority of the cases with DPB till date have been described from East Asian countries but sporadic reports from western population have also been published.[4,5] The aetiology of DPB is still not clear but the finding of DPB among East Asians, including Asian emigrants, indicates an effect of ethnicity and genetic predisposition to the disease. This stimulated a comprehensive search for associations between HLA types and this disease. Sugiyama *et al*[6] demonstrated a 63% positivity of the HLA-Bw54, which a serotype predominantly found in East Asians,[7] among 38 patients with DPB, compared with 11% of control subjects. This connection was later confirmed in a more extensive case-control study (odds ratio 3.4.).[8] Although Indian subcontinent is part of Asia, strangely however, to the best of our knowledge, this is the first confirmed case of DPB being reported from India. This may be an effect of lack of recognition and under-reporting of the disease. Another reason may be the fact that Indians have different ethnic background and are grouped with Caucasians and not with Asians.

It has also been suggested that surgical lung biopsy is often necessary to establish the diagnosis in areas where the prevalence of this entity is low but this CT pattern can be seen in various conditions. Therefore, the key stone to diagnosis is a high index of suspicion and adequate clinico-pathological correlation. In our patient, the main indicator which led us to investigate the patient extensively was a history of cough with copious expectoration coupled with rapid worsening of symptoms in a short duration. History of recurrent sinusitis was only obtained in retrospect and our patient

fulfilled all the first three and two of the last three criteria for the diagnosis.[3] But as mentioned above, surgical lung biopsy was performed to confirm the diagnosis which showed widespread transmural and peribronchial infiltration by lymphocytes, plasma cells and histocytes. A prominent involvement of respiratory bronchioles, a distinctive feature of DPB was also identified in contrast to other forms of obliterative bronchiolitis in which membranous bronchioles are involved. All other causes which mimic DPB were ruled out with relevant serological and biochemical investigations.

The HLA serotyping could have given the answer to the question whether our patient carried the predisposing HLA serotype like most of the patients with DPB in East Asia. But it could not be done because of logistic reasons.

In conclusion, DPB is a potentially treatable cause of bronchiectasis and a high index of suspicion is required to establish the diagnosis. All patients presenting with a suggestive symptom complex should be thoroughly investigated before considering idiopathic bronchiectasis as the aetiology.

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