CASE REPORT

Diffuse Pan Bronchiolitis Presenting with Bronchiectasis: A Case Report

Swathi Karanth M. P[1], Ketaki Utpat[1], Unnati Desai[1], Jyotsna M. Joshi[1]*

[1]Department of Pulmonary Medicine, T. N. Medical College, B. Y. L. Nair Hospital, Mumbai-400008 (Maharashtra) India

Abstract:

Diffuse Pan Bronchiolitis (DPB) is a peculiar airway disease with its pathogenesis enrooted in a complex interplay of various genetic and environmental factors. Airway inflammation, chronic airflow limitation and suppuratives in pulmonary infections are the distinctive features of this entity. It poses a close differential to other frequently encountered pulmonary conditions like chronic bronchitis, emphysema, bronchiectasis and constrictive bronchiolitis. Deferment in diagnosis can culminate in irreversible airway remodeling and progressive respiratory failure. Hence a punctual recognition is vital. Macrolide group of drugs are prime modality of therapy and the response to therapy is benignant. We herein describe a case of DPB with development of sequelae owing to its delayed detection.

Keywords: Bronchiectasis, Diffuse pan bronchiolitis, Macrolides

Introduction:

Diffuse Pan Bronchiolitis (DPB) is a rare entity characterized by chronic airflow obstruction and diffuses nodular lesions on High Resolution Computed Tomography (HRCT). Various respiratory diseases like Allergic Bronchopulmonary Aspergillosis (ABPA), respiratory bronchiolitis-interstitial lung disease, obliterative bronchiolitis, hypersensitivity pneumonia etc. mimic DPB in clinical and radiological manifestation. However, the criteria for DPB laid down by Ministry of Health Welfare, Japan [1]. Table 1 has eased the diagnostic difficulty. Prompt diagnosis and appropriate management are vital at early stages to prevent irrevocable complications like bronchiectasis, and progressive respiratory failure. Hereby we report an advanced case of DPB which presented to our hospital with bronchiectasis.

Table 1: Criteria for Diffuse Pan Bronchiolitis by Ministry of Health Welfare, Japan

Persistent cough, sputum and exertional dyspnoea
History of chronic paranasal sinusitis
Bilateral diffuse small nodular shadows on a plain chest radiography film or centrilobular micronodules on chest computed tomography images
Coarse crackles
FEV_1/FVC <70% and $P_{a,O2}$ <80 mmHg
Titre of cold haemagglutinin ⩾64

Definite cases should fulfil criteria 1, 2 and 3, along with at least two of criteria 4, 5 and 6.
FEV_1: Forced Expiratory Volume in one second; FVC: Forced Vital Capacity; $P_{a,O2}$: Arterial Oxygen Tension.

Case Report:

A 70 year old nonsmoker woman presented to our hospital with five year history of cough with copious mucoid expectoration, recurrent rhinosinusitis and dyspnoea on exertion Grade 1 (as per Modified Medical Research Council grading). She was treated symptomatically and in view of non-relief of symptoms she visited our hospital. Her general physical examination revealed tachycardia and tachypnoea. There were signs of hyperinflation with bilateral crepitations on respiratory system examination. Laboratory investigations revealed normal haemogram, liver and kidney function tests except for dyslipidemia. Serum Immunoglobulin (IgE) was elevated (553 IU/L), however specific IgE for *Aspergillus fumigatus* was negative. Cold Agglutinin and Rheumatoid Factor (128 U/L) were positive. Arterial Blood Gas (ABG) analysis showed mild hypoxemia (PaO_2-72 mm Hg). Six minute walk distance was 220 m and there was significant post exercise desaturation (SPO_2-92% to 84%). Chest radiograph revealed bilateral reticulonodular opacities. HRCT showed bilateral diffuse centrilobular nodules associated with bilateral hyperinflation and bilateral tubular bronchiectasis. Maxillary sinusitis was evident on radiograph of paranasal sinus. Spirometry was suggestive of obstructive abnormality with ratio of Forced Expiratory Volume in First Second (FEV1) to Forced Vital Capacity (FVC) of 61 percent with post bronchodilator FEV1 of 0.62 L i.e. 40% predicted. Echocardiography revealed mild pulmonary hypertension (PASP as estimated by TR jet of 40 mm Hg). There was no tracheobronchial abnormality on bronchoscopy. Sputum for acid fast bacillus was negative. Diagnosis of DPB was made as patient fulfilled Ministry of Health Welfare, Japan's diagnostic criteria. She was treated with bronchodilators and was started on oral azithromycin 250 mg daily. She was given influenza and pneumococcal vaccination and postural drainage techniques and breathing exercises were taught. Patient was discharged after clinical stabilization. (Fig. 1)

Discussion:

DPB is an idiopathic disease characterized by chronic inflammation of respiratory bronchioles. The term DPB was coined by Yamanka *et al.* [2] in 1969; however, it gained importance from international scientific community in 1980s. After its initial description from Japan, several cases were encountered in eastern World and other parts of Asia. Currently, DPB is a well-recognized entity worldwide.

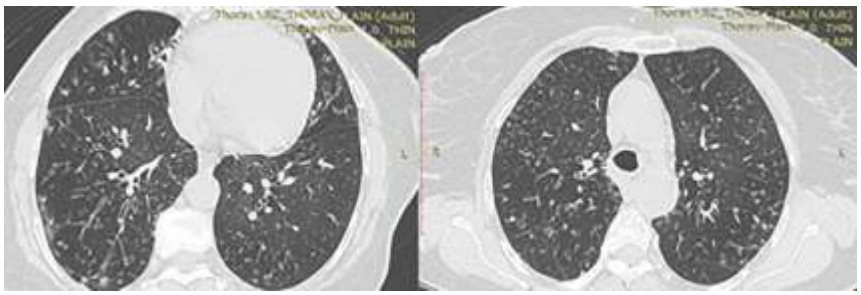

Fig. 1: HRCT Thorax showing Bilateral Diffuse Centrilobular Nodules and Bronchiectasis

The term diffuse refers to bilateral lung involvement and pan refers to involvement of all three layers of respiratory bronchioles. Exact etiology of the disease is unclear, however, association of HLA–A loci and HLA-B loci has been identified. Keicho *et al.* [3] have suggested probable HLA-B locus on chromosome 6p 21.3. An accumulation of activated neutrophils along with T lymphocytes and cytokine particularly IL-8 in the airways appears to be an important pathogenic mechanism and increased MUC5B gene expression contributes to hyper secretary airway disease [4]. Histologically, DPB is characterized by chronic inflammation, affecting respiratory bronchioles and adjacent centrilobular regions, with infiltration of foamy macrophages, neutrophils and lymphocytes. Clinically, the disease can affect any age group however, the development of symptoms typically occurs in the second to fifth decade [5] with slight male predilection (M: F -2:1) [2]. Our patient, however, was a geriatric with late onset of her symptoms. DPB manifests with chronic productive cough and dyspnea. Studies reported 84.8% prevalence of chronic pansinusitis in DPB [5]. Physical examination reveals crackles in more than 80% of patients, wheezes or both. In untreated patients, DPB progresses to bronchiectasis, respiratory failure and death. In our patient, bronchiectasis had already set in by the time she presented to us.

Imaging studies like chest radiography shows bilateral, diffuse, nodular shadows in more than 70% initially, and in more than 90% of patients at a later stage [6]. Features suggestive of hyper-inflation and bronchiectasis may also be evident in advanced cases. HRCT findings include centrilobular nodules, peripheral air trapping, dilatation of airways and bronchial wall thickening. DPB is graded into 4 stages on the basis of HRCT findings [6]. Stage 1 includes small nodules (5 mm in diameter) at the end of bronchovascular branching structures. Stage 2 is characterized by centrilobular nodules with tree-in-bud appearance. Cystic dilatations of these nodules represent stage 3. Stage 4 is characterized by large cysts that are connected to dilated proximal bronchi. The most characteristic and diagnostic laboratory features associated with DPB are persistent elevation of cold agglutinins, elevated serum IgA, mild neutrophilia, raised erythrocyte sedimentation and C-reactive protein. Positive rheumatoid factor is a frequent association. ABG may suggest hypoxia and spirometry reveals significant airflow limitation resistant to bronchodilators. Cut-off points of lung functions for diagnosis are decreased forced expiratory volume in one second/forced vital capacity less than 70%, vital capacity <80% predicted and residual volume <150% predicted [7]. Diagnosis of DPB is made if cases fulfil first three mandatory criteria along with at least two of the subsequent optional criteria (Table 1).

Management comprises of long term macrolide therapy for initial six months with subsequent clinico-radiological assessment [8]. The mechanism of macrolide efficacy in this entity is attributed to their anti-inflammatory and immunomodulatory action. Therapy can be stopped after 2 years once clinical and radiological findings improve and pulmonary function stabilizes. Therapy should be continued for more than 2 years in advanced disease. Prognosis of DPB has improved with long term macrolide treatment. Early diagnosis and treatment initiation have shown to improve clinical symptoms and reverse nodular shadows and normalize

pulmonary function and cold agglutinin titre [9]. Our patient satisfied all the clinicoradiological, serological and pulmonary function diagnostic criteria and was a prototype case of this meagerly recognized disease. Delayed diagnosis in her had resulted in progression of disease to succeeding stage which was irreversible.

Conclusion:

We emphasize that DPB is a curable disease with opportune diagnosis and therapy. Clinicians need to maintain a heightened index of suspicion for this entity which has a huge clinicoradiological camouflage with other more habitually encountered airway diseases.

References

1. Nakata K. Revision of clinical guidelines for diffuse pan bronchiolitis. Annual report on the study of diffuse lung disease in 1998. Grant-in Aid from the Ministry of Health and Welfare of Japan. Tokyo, 1999: 109-111.
2. Homma H, Yamanaka A, Tanimoto S, Tamura M, Chijimatsu Y, Kira S, *et al*. Diffuse pan bronchiolitis. A disease of the transitional zone of the lung. *Chest* 1983; 83(1):63-9.
3. Keicho N, Ohashi J, Tamiya G, Nakata K, Taguchi Y, Azuma A, *et al*. Fine localization of a major disease-susceptibility locus for diffuse panbronchiolitis. *Am J Hum Genet* 2000; 66(2):501-7.
4. Kamio K, Matsushita I, Hijikata M, Kobashi Y, Tanaka G, Nakata K, *et al*. Promoter analysis and aberrant expression of the MUC5B gene in diffuse panbronchiolitis. *Am J Respir Crit Care Med* 2005; 171(9):949-57.
5. Poletti V, Casoni G, Chilosi M, Zompatori M. Diffuse pan bronchiolitis. *Eur Respir J* 2006; 28(4): 862-71.
6. Akira M, Kitatani F, Lee YS, Kita N, Yamamoto S, Higashihara T, *et al*. Diffuse pan bronchiolitis: evaluation with high-resolution CT. *Radiology* 1988; 168(2):433-8.
7. Honma H. Diffuse panbronchiolitis. *Nihon Kyobu Shikkan Gakkai Zasshi* 1975; 13:383-95. (Japanese).
8. Kudoh S, Azuma A, Yamamoto M, Izumi T, Ando M. Improvement of survival in patients with diffuse panbronchiolitis treated with low-dose erythromycin. *Am J Respir Crit Care Med* 1998; 157(6 Pt 1):1829-32.
9. Kudoh S, Uetake T, Hagiwara K, Hirayama M, Hus LH, Kimura H, *et al*. Clinical effects of low-dose long-term erythromycin chemotherapy on diffusepanbronchiolitis. *Nihon Kyobu Shikkan Gakkai Zasshi* 1987; 25:632-42 (Japanese).

[*] ***Author for Correspondence:*** *Dr. Jyotsna M. Joshi, Department of Pulmonary Medicine , TNMC & BYL Nair Hospital, AL Nair Road, Mumbai Central, Mumbai- 400008. Email- drjoshijm@gmail.com Phone- 02223003095*