Diffuse panbronchiolitis in an Australian aborigine

James Brown & Graham Simpson

Department of Thoracic and Sleep Medicine, Cairns Base Hospital, Cairns, Queensland, Australia

Keywords
Australian aborigine, bronchiolitis, erythromycin, macrolide.

Correspondence
James Brown, Department of Thoracic and Sleep Medicine, Cairns Base Hospital, PO Box 902, Cairns, 4870 Queensland, Australia.
E-mail: drjamesbrown@gmail.com

Received: 18 December 2013; Revised: 29 December 2013; Accepted 06 January 2014

Respirology Case Reports 2014; 2(2): 64–66
doi: 10.1002/rcr2.50

Abstract
Diffuse panbronchiolitis (DPB) is a chronic sino-bronchial disease. It has remained restricted to the Japanese and cases in the West are unusual. We present a patient of Australian aboriginal origin with DPB. The known efficacy of low-dose erythromycin in DPB is again described. Chronic respiratory disease is common in the Australian aboriginal population and DPB should be considered in the differential.

Introduction
Diffuse panbronchiolitis (DPB) is a distinct clinicopathological syndrome that involves the upper and lower respiratory tracts. It occurs mainly in the Japanese and has rarely been reported outside of the Far East. We recently reported a series of Melanesians with DPB [1].

The diagnostic criteria proposed in 1998 by a working group of the Ministry of Health and Welfare of Japan are still useful for case definition:

(i) Persistent cough, sputum, and exertional dyspnea;
(ii) A history of, or current, chronic sinusitis;
(iii) Bilateral diffuse nodular shadows on plain chest x-ray or centrilobular micro nodules on chest computed tomography (CT);
(iv) Coarse crackles;
(v) FEV1/FVC <70% and PaO2 <80 mm Hg; and
(vi) Titer of cold hemagglutinin >64.

Definite cases should fill criteria 1, 2 and 3, and at least two of criteria 4, 5 and 6 [2, 3].

Low-dose erythromycin significantly improves the survival of patients with DPB. This macrolide improves symptoms, pulmonary function and hypoxemia, and increases the 10-year survival rate to >90% [4].

We present the first case of DPB described in an Australian aborigine.

Case Report
A 65-year-old Australian aboriginal man was referred to our clinic with “nodular lung disease,” as reported on a chest radiograph. He had been unwell for 3 months prior to his initial assessment, with breathlessness and a cough productive of mucoid sputum. He described a weight loss of 5 kg during this period, but no history of chest pain or hemoptysis. Sputum cultures had grown Haemophilus influenzae, Streptococcus pneumoniae, and Moraxella catarrhalis. He received oral antibiotic therapy, with multiple courses, and had little improvement in his symptoms.

He gave a history of chronic sinusitis for which he was on inhaled corticosteroids.

He had been diagnosed with “asthma” in 2003 and was compliant with an inhaled long-acting beta-agonist/corticosteroid combined inhaler and a long-acting anticholinergic inhaler.

The man was a lifelong nonsmoker. He had no history of tuberculosis contacts, and no avian or mulch exposure.

Clinical examination revealed a middle-aged aboriginal man with early digital clubbing. Auscultation of his chest
revealed diffuse coarse crackles and scattered expiratory rhonchi. There were no signs of right heart failure.

His chest radiograph at presentation showed a diffuse bilateral nodular infiltrate. A high resolution CT scan of the chest is shown in Figure 1. Two cuts, one just below the level of the carina (left) and one towards the lung bases, show a diffuse nodular infiltrate with extensive tree-in-bud change. There is centrilobular bronchiectasis with bronchial wall thickening, especially in the lower zones.

Detailed lung function tests are shown in Table 1. The initial tests show evidence of a severe obstructive ventilatory defect with hyperinflation. The gas transfer was mildly impaired, but corrected to normal for lung volumes.

The results of laboratory investigations are outlined in Table 2. The cold agglutinin and rheumatoid factor levels were both significantly elevated.

Table 1. Detailed lung function tests.

| Unit       | Reference | Pre-erythromycin | Post-erythromycin |
|------------|-----------|------------------|-------------------|
| Spirometry |           |                  |                   |
| FEV1       | Liters    | 2.96             | 1.20 (40)         |
| FVC        | Liters    | 3.78             | 2.08 (55)         |
| FEV1/FVC   | %         | 76               | 58                |
| Lung Volume|           |                  |                   |
| TLC        | Liters    | 6.51             | 5.53 (85)         |
| VC         | Liters    | 3.93             | 2.08 (53)         |
| RV         | Liters    | 2.40             | 3.45 (144)        |
| RV/TLC     | %         | 39               | 62                |
| FRC PL     | Liters    | 3.47             |                   |
| Diffusion  |           |                  |                   |
| DLCO       | mL/mm Hg/min | 25.8          | 16.7 (64)         |
| DLCO Adj   | mL/mm Hg/min | 25.8          | 16.7 (64)         |
| VA         | Liters    | 2.96             |                   |
| DLCO/VA    | mL/mm Hg/min/L | 5.17        | 5.63 (109)        |

DLCO = diffusing capacity for carbon monoxide, DLCO Adj = diffusing capacity for carbon monoxide adjusted for alveolar volume, FEV1 = forced expiratory volume in 1 sec, FRC PL = functional residual capacity, FVC = forced vital capacity, RV = residual volume, TLC = total lung capacity, VA = alveolar volume, VC = vital capacity.

Figure 1. High-resolution computed tomography scan of the thorax (two cuts).

| Test                  | Result                  |
|-----------------------|-------------------------|
| Cold agglutinin titer | 128 H titer (<32)       |
| Rheumatoid factor     | 138 IU/mL (<20)         |
| ANA                   | negative                |
| ANCA                  | negative                |
| HLA analysis (Class I serology) | A 24; A 34; B 56; B 60; Bv 6; Cw 1; Cw 3 |
| Ig G level            | 13.3 g/L (7.0–16.0)     |

ANA = anti-nuclear antibody, ANCA = ant-nuclear cytoplasmic antibody, HLA = human leukocyte antigen.

Treatment with low-dose erythromycin for 6 months improved his symptoms and his chest radiograph returned to normal. Repeat detailed lung function had improved dramatically (Table 1).
Discussion

We present the first case of DPB in an indigenous Australian man. The clinical, serological, and radiological criteria for the diagnosis of DPB are fulfilled. In addition, there was resolution of symptoms and significant improvement in both chest radiograph and lung function tests after treatment with low-dose macrolide.

With regard to other sino-bronchial syndromes that need exclusion in this case. Young’s syndrome is associated with obstructive azoospermia. Our patient is a parent. Good’s syndrome requires the presence of a thymoma and immunodeficiency. Our patient has normal immunoglobulin levels and no thymoma evident on CT scanning of the thorax. Human T-lymphotropic virus (HTLV) infection has been associated with bronchiectasis in indigenous patients in Central Australia. HTLV-1 serology was nonreactive in this case. Although formal nasal brushing and genetic studies were not performed, primary ciliary dyskinesia does not respond to macrolide therapy.

A genetic susceptibility to the disease has been shown in patients in the Far East. This is in the form of an association with human leukocyte antigen (HLA) class I antigens. HLA-B54 antigens are more commonly observed in the Japanese, Chinese, and Koreans with the condition [2, 5]. This particular genotype was not seen in our patient.

Chronic respiratory disease and bronchiectasis is common among aborigines. The etiology remains unclear and DPB may explain this.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

References

1. Brown J, and Simpson G. 2012. Diffuse panbronchiolitis in Melanesians. TSANZ Poster Abstracts. Respirology 17:42–87.
2. Keicho N, and Hijikata M. 2011. Genetic predisposition to diffuse panbronchiolitis. Respirology 16:581–588.
3. Crosbie PAJ, and Woodhead MA. 2009. Long-term macrolide therapy in chronic inflammatory airway diseases. Eur. Resp. J. 33:171–181.
4. Kanoh S, and Rubin BK. 2010. Mechanisms of action and application of macrolides as immunomodulatory medications. Clin. Micro. Rev. 23:590–615.
5. Sugiyama Y, Kudoh S, Maeda H, et al. 1990. Analysis of HLA antigens in patients with diffuse panbronchiolitis. Am. Rev. Resp. Dis. 141:1459–1462.