Diffuse panbronchiolitis in a Samoan man

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Abstract
Diffuse panbronchiolitis (DPB) is an idiopathic inflammatory disease which is predominantly recognised in the Japanese population with only isolated case reports in Western populations. This is the first reported case of DPB in a Samoan man with typical radiological and histopathological features. He had an excellent response to long-term erythromycin and this case highlights the importance of recognising this rare disease.

Introduction
Diffuse panbronchiolitis (DPB) is an idiopathic inflammatory disease that is well recognised in Japan and predominantly affects East Asians. The aetiology of DPB is unknown. However, given the high prevalence of DPB almost exclusively in East Asians it is thought there may be a genetic component [1]. No gender predominance or relationship to smoking has been determined [2]. There have only been case reports and small series documenting DPB in Western populations [1]. Within Australia there have been isolated cases of DPB in Melanesians and an Australian Aborigine [3,4]. However, there have been no reported cases of DPB in the Samoan population.

DPB is characterised by progressive obstructive airway disease and large volume sputum production. The characteristic pathological findings seen on biopsy are transmural and peribronchial infiltration by lymphocytes, plasma cells and histiocytes within the interalveolar septae surrounding the terminal respiratory bronchioles and alveolar spaces [1]. Without treatment, patients develop bronchiectasis and respiratory failure. Prior to the recognised response to erythromycin, the prognosis for patients with DPB in Japan was poor, with 5- and 10-year survival rates of 62.1 and 33.2% respectively. With long-term erythromycin treatment the 10-year survival rate has improved to >90%, highlighting the importance of recognising this condition [5].

Diagnostic criteria for DPB was proposed by a working group of the Ministry of Health and Welfare of Japan in 1998 (Table 1) [2]. Definite cases should fulfil the first three criteria in Table 1 and at least two of the other three remaining criteria. As DPB outside of the Japanese population is rare, the diagnosis in other populations is usually based on a histological diagnosis from a lung biopsy.

Case Report
A 25-year-old Samoan man who had lived in Australia and New Zealand was referred to the emergency department with a persistent cough and an abnormal chest X-ray. He had been diagnosed with asthma as a teenager with his main symptoms being exertional dyspnoea, a productive cough, and chronic sinusitis. He had been started on inhaled corticosteroids and bronchodilators with no improvement in his symptoms. The patient had no previous respiratory function tests or chest imaging. In the previous 2 months he had a persistent cough, producing half a cup of green-yellow sputum per day and worsening
exertional dyspnoea. He reported subjective fevers and 5 kg weight loss in the previous 3 months but no night sweats.

The patient was a lifelong non-smoker and worked in a mattress factory. He had lived in Australia for the last 10 years and prior to that in New Zealand. He was of Samoan heritage with no known East Asian ancestry. He had no known exposure to tuberculosis and no risk factors for immunosuppression.

On initial assessment of the patient, he appeared well with oxygen saturations of 99% on room air. The significant clinical examination findings were coarse crackles predominantly at the bases with no wheeze. He was systemically well and there was no evidence of right heart failure. His initial chest X-ray showed a bilateral nodular interstitial infiltrate involving the mid and lower zones. He underwent a high resolution computed tomography (HRCT) which showed extensive tree-in-bud changes within all lobes, but particularly the lower lobes where there was also bronchial wall thickening and evidence of early bronchiectasis (Fig. 1). Respiratory function tests showed fixed moderately severe airflow obstruction (Table 2). Sputum samples and bronchial washings were sent for microbiology. *Haemophilus influenzae* was isolated and mycobacterium cultures were negative. An autoimmune screen was negative. The patient then underwent a bronchoscopy and transbronchial biopsy. Histopathology showed chronic inflammatory infiltration of the lung.

**Table 1. Proposed diagnostic criteria for DPB.**

|   | Persistent cough, sputum, and exertional dyspnoea |
|---|---------------------------------------------------|
| 2 | A history of, or current chronic sinusitis        |
| 3 | Bilateral diffuse nodular shadows on plain chest X-ray or centrilobular micronodules on chest CT |
| 4 | Coarse crackles                                   |
| 5 | FEV₁/FVC <70% and PaO₂ < 80 mmHg                  |
| 6 | Titer of cold haemagglutinin >64                  |

DPB, diffuse panbronchiolitis; CT, computed tomography; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; PaO₂, partial pressure of oxygen.

![Figure 1. CT scan A & B show findings pre-treatment. CT scan C & D show findings after 3 months of Erythromycin therapy.](image)
interstitium, plus expansion of alveolar walls and interstitium by foamy histiocytes (CD68+), consistent with DPB (Fig. 2). Stains for fungal elements, acid fast organisms, and neoplasia were negative.

In light of the diagnosis of DPB further investigations were performed. A computed tomography (CT) of the sinuses confirmed pan sinusitis with marked mucosal thickening in maxillary, ethmoidal, sphenoid, and frontal sinuses. The cold agglutinin titre and rheumatoid factor were within normal range but the IgA level was elevated at 8.1 g/L (reference range 1.0–4.0 g/L).

The patient was started on erythromycin 400 mg twice a day. Following 3 months of treatment, he reported a marked improvement in his exercise capacity, his productive cough had almost completely resolved, and he now had infrequent sputum production. He showed a good radiological improvement on HRCT (Fig. 1) and spirometry had also improved (Table 2). The patient currently remains on erythromycin ethylsuccinate with ongoing follow up under a respiratory physician.

### Table 2. Spirometry prior to treatment and after 3 months of macrolide therapy.

| Spirometry         | Pre-treatment (L) (% predicted) | 3 months post-treatment (L) (% predicted) | % Change |
|--------------------|--------------------------------|------------------------------------------|----------|
| FEV₁ (L)           | 2.59 (55)                      | 3.61 (76)                                | +28%     |
| FVC (L)            | 4.12 (71)                      | 5.04 (88)                                | +18%     |
| FEV₁/FVC           | 63                             | 71                                       |          |

FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

Discussion

This is the first case of DPB reported in a Samoan patient. His clinical history, as well as radiological findings and respiratory function tests were all consistent with DPB. Elevated IgA, cold agglutinins, and rheumatoid factor have all been associated with DPB. However in this case only the IgA was elevated. A lung biopsy is not part of the diagnostic criteria proposed by a working group of the Ministry of Health and Welfare in Japan in 1998 [2]. However most case reports of DPB outside of the Japanese population have been confirmed with a biopsy. In this case the histopathological findings confirmed the diagnosis of DPB.

Although the aetiology of DPB is unknown there is thought to be a genetic predisposition given its high prevalence in East Asian populations. HLA-Bw54 antigen has been shown to be associated with DPB in the Japanese population and HLA-A11 antigen has been associated with DPB in Korean patients [1]. We did not perform HLA testing in this patient.
Both cystic fibrosis (CF) and primary ciliary dyskinesia (PCD) are differential diagnoses that need to be considered when diagnosing DPB as they share some clinical similarities. DPB is not associated with elevated sweat chloride tests or pancreatic insufficiency, and generally the high sputum burden seen in DPB is uncommon in CF [2]. In addition, DPB is also not associated with the spectrum of cilia abnormalities seen in PCD or infertility in males [2]. In this case, given the diagnosis of DPB was made on lung biopsy, further testing for CF and PCD was not performed.

This patient has shown an excellent response both symptomatically and radiologically after 3 months of treatment with erythromycin. He will require ongoing follow up after completion of therapy given the relatively unknown natural history of this disease. This case highlights the importance of clinicians being aware of DPB despite it being rare as the prognosis without macrolide therapy is poor.

Disclosure Statements
No conflict of interest declared. Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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