<table>
<thead>
<tr>
<th>Title</th>
<th>Clinical profiles of chinese patients with diffuse panbronchiolitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author(s)</td>
<td>Tsang, KWT; Ooi, CGC; Ip, MSM; Lam, WK; Ngan, H; Chan, EYT; Hawkins, B; Ho, CS; Amitani, R; Tanaka, E; Itoh, H</td>
</tr>
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Kenneth W T Tsang, Clara G C Ooi, Mary S M Ip, Wah-kit Lam, Henry Ngan, Eric Y T Chan, Brian Hawkins, Chu-shak Ho, Ryoichi Amitani, Eisaku Tanaka and Harumi Itoh

Thorax 1998;53;274-280

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Clinical profiles of Chinese patients with diffuse panbronchiolitis

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Abstract

Background—Diffuse panbronchiolitis (DPB), characterised by progressive sinusobronchial sepsis, is well characterised in Japanese subjects but not in other ethnic groups. The experience with DPB in seven Chinese patients is described and the clinical profiles compared with those of Japanese subjects.

Methods—Seven Chinese patients (three women; mean (SD) age 48 (18.6) years, all never smokers) who attended a teaching hospital centre and fulfilled the diagnostic criteria for DPB were assessed prospectively for clinical, radiological, lung function, microbiological, and other “characteristic” laboratory parameters.

Results—Lung function assessment showed a typical obstructive pattern (n = 5) and air trapping (n = 7). Typical bronchiolar infiltration by lymphocytes and plasma cells and accumulation of foamy macrophages in the intraluminal tissue were detected in open lung biopsy specimens (n = 2). Chest radiographs and high resolution computed tomographic scans revealed hyperinflation, diffuse nodules, bronchial thickening and dilatation, and peribronchiolar accumulation of foamy macrophages. Pathologically, thickening of the bronchiolar wall due to infiltration by lymphocytes, plasma cells and histiocytes, and peribronchiolar accumulation of foamy macrophages occur. DPB is distinct from asthma, bronchiectasis, and chronic obstructive pulmonary disease pathologically and radiologically although some of the clinical symptoms can overlap.

Although DPB is not an uncommon disease amongst Japanese subjects, only sporadic cases have been reported in Caucasians, Koreans, Indians, and Hispanics. HLA-B54 is found in 63.2% of Japanese patients with DPB (relative risk 13.3) and has been reported in a widely quoted study to be prevalent in 10.4% of Chinese subjects.

This suggests that the Chinese might also be susceptible to developing DPB. However, there has been no systematic study on DPB in Chinese subjects in whom it is still rarely reported and poorly defined. Under-recognition of this condition, which mimics primary ciliary dyskinesia, bronchiectasis, and cystic fibrosis, has serious consequences as DPB is highly responsive to treatment with low doses of erythromycin but is fatal if untreated. Although firmly established, the diagnostic criteria for DPB were constructed according to the characteristics of Japanese patients and have not been validated for other ethnic groups. We therefore report our experience with DPB in seven well characterised Chinese patients and compare the clinical profiles of our patients with those of the Japanese.

Methods

PATIENT POPULATION

Between October 1994 and October 1996 seven patients (pure southern Chinese) were diagnosed to have DPB at the Department of Medicine, University of Hong Kong. Diagnosis was made according to established diagnostic criteria and after consultation with clinicians and radiologists experienced in DPB. An informal survey through the clinical practice of
### Table 1 Diagnostic criteria for diffuse panbronchiolitis

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
<th>Physical examination</th>
<th>Sputum pathogen</th>
<th>Other</th>
<th>Diagnostic criteria for diffuse panbronchiolitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>Wheezing</td>
<td>Hyperinflation</td>
<td><em>H. influenzae</em></td>
<td>None</td>
<td>FEV₁ &lt;70% predicted or FEV₁/FVC &lt;70%</td>
</tr>
<tr>
<td>Sputum production</td>
<td>Crackles</td>
<td>Lower zone distribution</td>
<td><em>P. aeruginosa</em></td>
<td>None</td>
<td>RV &gt;150% predicted</td>
</tr>
<tr>
<td>Dyspnea on exertion</td>
<td>Crackles</td>
<td>Hyperinflation</td>
<td><em>M. pneumoniae</em></td>
<td>None</td>
<td>VC &lt;80% predicted</td>
</tr>
<tr>
<td>None</td>
<td>None</td>
<td>Hyperinflation</td>
<td><em>C. pneumoniae</em></td>
<td>None</td>
<td>Pao₂ &lt;80 mm Hg (∼10.6 kPa)</td>
</tr>
</tbody>
</table>

#### INVESTIGATION PROFILES

Lung function indices were measured using a Sensor-Medics 2200 Lung Function package and standard protocol as per routine clinical practice. Nasal mucosa was obtained from the inferior turbinate of subjects with a cytology brush (without anaesthetic) and resuspended in medium 199 (Flow Laboratory, Paisley, Scotland, UK) before examination of ciliary movement and beat frequency with a Leica DM LB phase contrast microscope (Leica, Wetzlar, Germany) and a MPV-COMBI (Leica, Wetzlar, Germany) photomultiplier system as described previously.

Ciliated epithelium was fixed in 2.5% glutaraldehyde (in osmium tetroxide buffer) and embedded in araldite for ultrastructural examination by a trained electron microscopy technician.

Evaluation of routine haematological indices and renal and liver biochemical profiles; serum immunoglobulin (Ig) G, IgA, and IgM; autoantibody titres (for rheumatoid factor, antinuclear factor, and IgG against Ro, La, Jo₁, mitochondrial, and smooth muscle); arterial blood gas tensions; serum IgG subclasses; lymphocyte subset analysis; α₁-antitrypsin level; viral titres (measles, mumps, influenza, parainfluenza, respiratory syncytial, adenovirus, rotavirus, and enterovirus); blood CD4/CD8 lymphocyte ratio; IgG against *Pseudomonas*

### Table 2 Characteristics of patients at presentation

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>1(M)</th>
<th>2(M)</th>
<th>3(F)</th>
<th>4(M)</th>
<th>5(M)</th>
<th>6(F)</th>
<th>7(F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset (years)</td>
<td>54</td>
<td>28</td>
<td>32</td>
<td>60</td>
<td>63</td>
<td>64</td>
<td>72</td>
</tr>
<tr>
<td>No. of months on treatment</td>
<td>57</td>
<td>30</td>
<td>32</td>
<td>61</td>
<td>64</td>
<td>64</td>
<td>73</td>
</tr>
<tr>
<td>Nasal symptoms (years)</td>
<td>30</td>
<td>15</td>
<td>15</td>
<td>None</td>
<td>50</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Sputum pathogen</td>
<td><em>H. influenzae</em></td>
<td><em>P. aeruginosa</em></td>
<td>Commensals</td>
<td><em>H. influenzae</em></td>
<td><em>P. aeruginosa</em></td>
<td><em>Mycoplasma tuberculosis</em></td>
<td><em>H. influenzae</em></td>
</tr>
<tr>
<td>Travel history to Japan</td>
<td>Nil</td>
<td>15 years before</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>11 years before</td>
<td>Nil</td>
</tr>
<tr>
<td>Medication</td>
<td>Atenolol</td>
<td>Hypertension</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Neurofibroma T8</td>
</tr>
<tr>
<td>Concurrent illness</td>
<td>Renal transplant</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Ciliary beat frequency</td>
<td>12</td>
<td>12</td>
<td>9.7</td>
<td>14.1</td>
<td>14.1</td>
<td>12.2</td>
<td>10.1</td>
</tr>
<tr>
<td>Serum IgA (90–450 mg/dl)*</td>
<td>268</td>
<td>224</td>
<td>614</td>
<td>420</td>
<td>368</td>
<td>365</td>
<td>465</td>
</tr>
<tr>
<td>CD4/CD8 ratio (0.63–3.24)*</td>
<td>1.98</td>
<td>0.57</td>
<td>3.55</td>
<td>3.7</td>
<td>1.58</td>
<td>0.78</td>
<td>1.88</td>
</tr>
<tr>
<td>IgG against <em>M. pneumoniae</em></td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>HLA typing</td>
<td>A2, B5, B60, DR9, DR11</td>
<td>A2, A33, B17, DR9, DR15, DR3</td>
<td>DR9, DR12</td>
<td>A2, A24, B55</td>
<td>A2, B46, B35</td>
<td>A24, B60</td>
<td>A24, A11, B27, DR13, DR15</td>
</tr>
<tr>
<td>Histological examination</td>
<td>TBB</td>
<td>Nil</td>
<td>Nil</td>
<td>TBB+OLB</td>
<td>TBB+OLB</td>
<td>TBB+OLB</td>
<td>TBB+OLB</td>
</tr>
</tbody>
</table>

TBB and OLB=transbronchial and open lung biopsies, respectively.

* Normal range for data.
Table 3  Investigation profiles at presentation and re-assessment

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood leucocyte count (&lt;10^9/ml)</td>
<td>11.7 (11.8)</td>
<td>7.6 (6.5)</td>
<td>8.3 (7.2)</td>
<td>9.6 (7.0)</td>
<td>13.9 (9.1)</td>
<td>6.1 (6.4)</td>
<td>9.0 (5.8)</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>29 (47)</td>
<td>84 (142)</td>
<td>41 (64)</td>
<td>57 (98)</td>
<td>22 (25)</td>
<td>53 (54)</td>
<td>44 (86)</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>61 (92)</td>
<td>95 (143)</td>
<td>52 (85)</td>
<td>67 (114)</td>
<td>35 (42)</td>
<td>45 (109)</td>
<td>101 (87)</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>29 (39)</td>
<td>74 (83)</td>
<td>69 (77)</td>
<td>63 (63)</td>
<td>47 (60)</td>
<td>60 (44)</td>
<td>38 (71)</td>
</tr>
<tr>
<td>RV/TLC (%)</td>
<td>212 (180)</td>
<td>147 (116)</td>
<td>167 (131)</td>
<td>270 (164)</td>
<td>101 (90)</td>
<td>144 (156)</td>
<td>164 (185)</td>
</tr>
<tr>
<td>KCO (% predicted)</td>
<td>84 (101)</td>
<td>101 (82)</td>
<td>105 (106)</td>
<td>111 (50)</td>
<td>37 (55)</td>
<td>39 (97)</td>
<td>96 (70)</td>
</tr>
<tr>
<td>PaO2 (kPa)*</td>
<td>8.3 (10.2)</td>
<td>12 (11.4)</td>
<td>9.3 (10.3)</td>
<td>8.2 (10.5)</td>
<td>8.0 (9.8)</td>
<td>8.1 (10.0)</td>
<td>9.0 (11.0)</td>
</tr>
<tr>
<td>C reactive protein (&lt;1mg/dl)</td>
<td>&lt;0.3 (&lt;0.3)</td>
<td>&lt;0.3 (&lt;0.3)</td>
<td>0.6 (&lt;0.3)</td>
<td>&lt;0.3 (&lt;0.3)</td>
<td>0.6 (&lt;0.3)</td>
<td>&lt;0.3 (&lt;0.3)</td>
<td>&lt;0.3 (&lt;0.3)</td>
</tr>
<tr>
<td>RV (% predicted)</td>
<td>64 (76)</td>
<td>93 (140)</td>
<td>66 (110)</td>
<td>70 (119)</td>
<td>37 (55)</td>
<td>39 (97)</td>
<td>96 (70)</td>
</tr>
<tr>
<td>VC (% predicted)</td>
<td>64 (101)</td>
<td>101 (82)</td>
<td>105 (106)</td>
<td>111 (50)</td>
<td>37 (55)</td>
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<td>8.2 (10.5)</td>
<td>8.0 (9.8)</td>
<td>8.1 (10.0)</td>
<td>9.0 (11.0)</td>
</tr>
</tbody>
</table>

Data shown are measurements made at presentation and re-assessment (in parentheses).
*Normal range for arterial blood gases when breathing room air 10.6–14 kPa.

Table 4 Radiological assessment at presentation and re-assessment

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood leucocyte count (×10^9/ml)</td>
<td>60 (20)</td>
<td>30 (0)</td>
<td>10 (0)</td>
<td>20 (0)</td>
<td>30 (2)</td>
<td>25 (5)</td>
<td>100 (50)</td>
</tr>
<tr>
<td>RV (% predicted)</td>
<td>212 (180)</td>
<td>147 (116)</td>
<td>167 (131)</td>
<td>270 (164)</td>
<td>101 (90)</td>
<td>144 (156)</td>
<td>164 (185)</td>
</tr>
<tr>
<td>VC (% predicted)</td>
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<td>66 (110)</td>
<td>70 (119)</td>
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</tr>
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<td>105 (106)</td>
<td>111 (50)</td>
<td>37 (55)</td>
<td>39 (97)</td>
<td>96 (70)</td>
</tr>
<tr>
<td>PaO2 (kPa)*</td>
<td>6.2 (7.2)</td>
<td>13.9 (9.1)</td>
<td>13.9 (9.1)</td>
<td>13.9 (9.1)</td>
<td>13.9 (9.1)</td>
<td>13.9 (9.1)</td>
<td>13.9 (9.1)</td>
</tr>
<tr>
<td>C reactive protein (&lt;1mg/dl)</td>
<td>&lt;0.3 (&lt;0.3)</td>
<td>&lt;0.3 (&lt;0.3)</td>
<td>0.6 (&lt;0.3)</td>
<td>&lt;0.3 (&lt;0.3)</td>
<td>0.6 (&lt;0.3)</td>
<td>&lt;0.3 (&lt;0.3)</td>
<td>&lt;0.3 (&lt;0.3)</td>
</tr>
<tr>
<td>VC (% predicted)</td>
<td>64 (101)</td>
<td>101 (82)</td>
<td>105 (106)</td>
<td>111 (50)</td>
<td>37 (55)</td>
<td>39 (97)</td>
<td>96 (70)</td>
</tr>
</tbody>
</table>

Data shown are measurements made at presentation and re-assessment (in parentheses).
*Normal range for arterial blood gases when breathing room air 10.6–14 kPa.

Radiological Assessment
All seven patients underwent thoracic HRCT scanning at the time of diagnosis and re-assessment (after 8.6 (9.4) months of erythromycin therapy) and were scanned in the supine position (scan thickness 1mm or 1.5mm and venous confluence to bases). Six lung zones were therefore evaluated individually for each patient. HRCT scans were graded as described previously by Akira et al.\(^9\): type 1, nodules associated with bronchovascular branchings; type 2, nodules branching in appearance ("tree-in-bud"); type 3, nodules connected to ring-shaped or ductal opacities (bronchiolitis); and type 4, dilatation of proximal terminal bronchioles and bronchi (predominantly at the peripheral airways).\(^9\) Distribution (diffuse or localised), symmetry, profusion of nodules, and areas of hypoattenuation and air trapping (on expiratory HRCT scans) were also assessed. Grading for nodular profusion, hypoattenuation, and air trapping was made according to the extent of involvement in each lung zone as: 0 (normal), 1 (<25% of lung zone involvement), 2 (>25% but <50%), and 3 (>50%). Bronchial dilatation was similarly graded by comparing bronchial calibre with that of the accompanying artery: 0 (normal bronchial calibre), 1 (<1.5 times calibre of accompanying artery), 2 (>1.5 but <2.0 times), and 3 (>2 times). Bronchial thickening was graded as 1 (mild), 2 (moderate), and 3 (severe). For each

pseudomallei, Legionella pneumophila, Chlamydia psittaci, Mycoplasma pneumoniae, and human adult T cell leukaemia virus (HTLV-1); Aspergillus precipitins; serum cold haemagglutinin; complements 3 and 4; sputum microbiology (routine aerobic and anaerobic, mycobacterial and fungal cultures), and full human leucocyte antigen (HLA) typing were performed at the Biochemistry, Haematology, Clinical Immunology, Microbiology, and Tissue Typing departments of the University of Hong Kong using routine methods. Density gradient sedimentation with Lymphoprep (Nycomed, Oslo, Norway) and ammonium chloride were used to remove the mononuclear and red cells in leucocyte-rich concentrate obtained from heparinised blood mixed with 6% dextran. Cytospins of granulocytes were fixed in absolute alcohol at 4°C for five minutes. Serum samples were diluted (1:20) in phosphate buffered saline and anti-neutrophil cytoplasmic antibody (ANCA) binding was detected by rabbit anti-human IgG-FITC conjugate (Dako, Glostrup, Denmark).\(^15\)

References
2. Nakata, radiographic grading\(^23\).
3. Akira et al.\(^9\).
4. Nodular dilatation, overall score
5. Bronchial dilatation, overall score
6. Airway dilatation, overall score
7. Hypoattenuation, overall score
8. Air trapping, overall score

Data shown are measurements made at presentation and re-assessment (in parentheses).
*Assessment made at expiratory HRCT scanning of the thorax.
NP=not performed.

Please refer to text for the scoring systems.
of these features an overall score was obtained by dividing the sum of the scores from all lung zones by six.

Chest radiographs corresponding in time to the HRCT scans were graded from types I to V as described by Nakata et al.24 Types I, II, III, IV, and V were assigned when there was overinflation without nodular shadows, disseminated small nodular shadows confined to one lung, small nodular shadows in both lungs, ring-shaped or tramline shadows in the lower lungs with nodular shadows, and large ring-shaped and nodular shadows, respectively.

Results

DEMOGRAPHIC DATA

The mean (SD) ages at onset of symptoms and at initial assessment were 48 (18.6) and 50 (17.8) years. None of the seven patients (three women) had ever smoked cigarettes and they received treatment with erythromycin (250 mg twice daily) for 8.6 (9.4) months before re-assessment. Three patients had travelled to Japan 15, 11, and 10 years before the onset of symptoms (table 2).

INVESTIGATION PROFILES

All the patients underwent the investigation profiles listed above and repeated measurements were made on some selected parameters as shown in table 3. At initial presentation the mean (SD) forced expiratory volume in one second (FEV1), forced vital capacity (FVC), residual volume (RV), vital capacity (VC), carbon monoxide transfer coefficient (Kco), and arterial oxygen tension (Pao2) were 46.3 (21.4)%, 65.1 (24.8)%, 172.1 (54.4)%, 66.4 (23.2)%, 105.7 (17.2)%, and 9.0 (1.4) kPa, respectively, which changed to 73.7 (38.7)%, 95.7 (31.3)%, 146 (35.0)% , 95.3 (30.0)%, 107.9 (22.1)% , and 10.5 (0.6) kPa after erythromycin therapy. Tests for ciliary beat movement and frequency, ciliary ultrastructure, HLA typing, α1-antitrypsin, viral titres, IgG against P pseudomallei, L pneumophilia, C psittaci, M pneumoniae, and HTLV-1, Aspergillus precipitins, complements 3 and 4, and routine haematological and biochemical indices were negative or normal at initial presentation. Serum IgA and IgG levels were persistently raised in two and three patients, respectively, although the levels of other immunoglobulins were normal. Antinuclear factor was positive in six patients and anti-smooth muscle in two, while anti-dsDNA, anti-extractable nuclear antigen, rheumatoid factor, and anti-mitochondrial antibodies were negative in all patients. ANCA (cytoplasmic) was positive in six patients, none of whom had anti-proteinase
subjects quoted in the literature does not
The 10% prevalence of HLA-54 in Chinese
most of our patients in possessing HLA-A2.4
HLA-B54 but shared a common feature with
sinobronchial sepsis and most had persistence
to treatment (figs 1 and 2).

RADIOLOGICAL ASSESSMENT
At the initial assessment nodular distribution
with lower lobe predominance was bilateral
and diffuse in all except two cases, in whom it
was asymmetrical (table 4). After treatment
with erythromycin there was an overall
improvement in both bronchial thickening and
dilatation, but not in hypotention of the
peripheral areas. Air trapping was confirmed
on expiratory scans in only two cases at initial
presentation and in all seven cases after eryth-
romycin treatment. The serial Akira and
Nakata classifications remained unchanged in
four and six patients, respectively, and did not
appear to reflect the reduction in nodular per-
fusion which was the most significant response
to treatment (figs 1 and 2).

Discussion
All our patients presented with typical chronic
sinobronchial sepsis and most had persistence of
P. aeruginosa or H. influenzae in their sputum,
characteristic radiological features, and excel-
lent clinical and radiological response to macrolide therapy (tables 1–4). However, our
cases differ from the Japanese patients (table 1)
in several respects, primarily the absence of
HLA-B54 type. The Chinese patient men-
tioned briefly by Iwata et al did not possess
HLA-B54 but shared a common feature with
most of our patients in possessing HLA-A2.4
The 10% prevalence of HLA-54 in Chinese
subjects quoted in the literature does not
agree with our finding of a prevalence of 3% in
patients from southern China.25 If HLA-B54
has a pathological role in DPB, then this low
incidence of HLA-54 would explain the
relative scarcity of DPB in the Chinese popu-
ation, in addition to the probable underdiagnos-
sis and reporting. Five of the seven patients in
this series had HLA-DR9 compared with
29.2% in the normal population in Hong
Kong. Although the number of patients tested
is small, our preliminary results suggest that
future patients should also be tested for HLA-
DR9 and HLA-A2. Two of our patients also
had HLA-B55, which has also been reported to
be increased in a Japanese study.14

Three of our cases had raised IgG levels but
IgG levels were normal, whereas 30.8% of
Japanese patients were reported to have IgG1
deficiency.26 The other “atypical” features
include normal or low CD4/CD8 lymphocyte
ratio in five patients, absence of raised serum
IgA in five, and absence of raised serum IgG,
cold haemagglutinin and rheumatoid factor in
seven patients.1 A review of the cases in the lit-
erature of DPB in non-Japanese subjects
revealed a total of 19 Mongoloid (14 Chinese
and five Koreans) and 13 non-Mongoloid cases
who generally had not been systematically
evaluated.4–8 10 12 15 16–18 27 Of these, HLA-B54
was detected in only two cases in the former
and either not checked or not detected in the
latter group. In addition, raised levels of cold
haemagglutinin were found in two Hispanic
patients but not in the rest of the aforemen-
tioned 32 cases.5 13 The other investigation
profiles that were considered to be characteris-
tic and helpful in the diagnosis (table 1),
including CD4/CD8 lymphocyte ratio, serum
IgA level, IgG subclass analysis, and M. pneumoniae serology, were not evaluated in
these non-Japanese patients. Our results sug-
gest that these “additional” features (table 1)
might not be applicable in the diagnosis of
DPB in non-Japanese patients. The finding of a
positive ANCA in six of our patients is also
interesting and needs confirmation by other
workers, as this has not been reported previ-
ously in DPB.

The value of HRCT scans in assessing small
airways disease in DPB is clear and is substan-
tiated by pathological-radiological corre-
lation.25 26 29 This experience, however, is
limited to Japan, largely due to the relative
confinement of DPB to that country. Periph-
eral areas of hypotention on HRCT
scanning26–35 are non-specific indicator of air
trapping and reflect an underlying hyperinfla-
tion caused by narrowing of the small airways.29
In the only other series of patients with DPB
followed up by HRCT scanning after treat-
mament with erythromycin there was an improve-
ment in nodular profusion but not airway dil-
atation and peripheral hypotention.29 In
contrast, our findings suggest that there was
partial reversibility in bronchiolar dilatation
in our patients, although no corresponding im-
provement in the peripheral areas of hypo-
tention was evident. This might be due to
selective and more severe injury to the periphe-
ral airways resulting in sustained distal air
trapping, whilst the less affected central larger
airways recovered with erythromycin treat-
mament. However, in agreement with Akira et al,10
there was a universal reduction in nodular pro-
fusion in all our patients after erythromycin
treatment. This important feature in the radi-
ological follow up of these patients, which
appears to parallel the improvement in lung
function and clinical improvement, could not
be accurately represented in the Nakata
Diffuse panbronchiolitis in Chinese patients

Our study also highlights the relative insensitivity of plain radiography compared with HRCT scanning in assessing disease activity, particularly in small airway pathology. The usefulness of the Nakata radiographic and Akira HRCT classifications in this study therefore appears to be limited.

As with Japanese patients, our patients responded very well in terms of lung function indices, blood oxygenation, symptomatic relief, sputum production, and radiological evaluation to low dose, long term treatment with erythromycin.7 Whilst the efficacy of macrolides in treating DBP is well established, the mechanism(s) is still largely unknown. One possible mechanism is the reduction of pulmonary levels of interleukin 8 and leukotriene B4, which are potent chemotactic agents.8,9 This leads to a reduction in neutrophil influx into the airways and alveolar space20 which is known to cause airway destruction in chronic bronchial sepsis by various processes such as the release of human neutrophil elastase.10,11 It is also possible that erythromycin interferes with the formation of P aeruginosa biofilms which are important in its persistence in the airways.12 Until the precise mechanism is known, more specifically targeted treatment cannot be planned other than empirical treatment with macrolides. There appears to be a “class effect” in that most of the available macrolides including erythromycin, clarithromycin, roxithromycin, and azithromycin, are efficacious in DBP.13 For resistant cases recent in vitro and clinical evidence suggests that inhalation of indomethacin and otioprim bromide might be effective in reducing sputum production.14,15 Interestingly, three of our patients had travelled to Japan prior to the onset of symptoms, similar to the Hispanic man who developed DBP after extensive travels to Japan and South East Asia.16 However, the long interval between the journey to Japan and the onset of symptoms makes an aetiological link very unlikely in our patients. As in the cases in the Japanese literature, there was no identifiable aetiology for the onset of chronic bronchial sepsis or DBP in our patients. Our investigations have also effectively excluded all the known differential diagnoses for DBP including primary ciliary dyskinesia, bronchiectasis, chronic bronchiitis and emphysema, bronchiolitis obliterans, cystic fibrosis (not known to occur in Chinese), Wegener’s granulomatosis, malignant lymphoma, and bare lymphocyte syndrome.4

Whilst we have demonstrated characteristic features of DBP in all our cases, only four patients were examined histologically for features of DBP. Open lung biopsy specimens of patients who fulfilled the clinical diagnostic criteria for DBP might very occasionally show unclassified bronchiolitis and bronchiolectasis.22 However, in most instances the pathological changes in DBP correlate well with HRCT features and HRCT scanning is advocated and frequently used as the diagnostic tool in this condition,17 especially in Japan where clinicians and radiologists have considerable relevant experience. In practice, most patients with DBP in Japan are routinely diagnosed using high quality thoracic HRCT scans. The clinical and radiological response to erythromycin also gives very good circumstantial evidence to support the diagnosis of DBP.

We have reported seven cases of DBP who, despite typical clinical features, appear to have different investigation profiles from their Japanese counterparts. More experience needs to be gathered on non-Japanese patients to evaluate further the clinical characteristics of this macrolide responsive but otherwise progressive idiopathic pulmonary disease.

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