Effects of airway infection by *Pseudomonas aeruginosa*: a computed tomographic study

Katherine A Miszkiel, Athol U Wells, Michael B Rubens, Peter J Cole, David M Hansell

Abstract

**Background** – *Pseudomonas aeruginosa* commonly infects the airways of patients with bronchiectasis. A study was undertaken to examine the relationship between infection of the airways with this pathogen, the morphological pattern of bronchiectasis on thin section computed tomographic (CT) scanning, symptom duration, smoking habits of the patients, and the presence of airflow obstruction.

**Methods** – Thin section CT scans of 22 adult patients with bronchiectasis and concurrent sputum infected by *P. aeruginosa* (Pa +ve) and those of 45 randomly selected patients not infected by *P. aeruginosa* (Pa – ve) were analysed independently by two thoracic radiologists. Patients with cystic fibrosis were excluded. Each scan was scored at a lobar level for extent of bronchiectasis, severity of bronchial wall thickening and dilatation, predominant pattern of bronchiectasis, presence of mucus plugging, and degree of decreased attenuation of the lung parenchyma.

**Results** – The Pa +ve group had more extensive bronchiectasis and a greater degree of bronchial wall thickening and dilatation on the CT scan than the Pa – ve group; more extensive decreased attenuation was seen in the Pa +ve group. These findings were robust on multivariate analysis; decreased attenuation was also independently related to the duration of sputum production.

**Conclusion** – Patients with bronchiectasis infected by *P. aeruginosa* have more extensive and severe bronchiectasis on thin section CT scanning than those without *P. aeruginosa* infection. The bronchi and small airways are both involved, reflecting the end result of complex interactions between host airways and the numerous virulence factors produced by *P. aeruginosa*. (Thorax 1997;52:260–264)

Keywords: *Pseudomonas aeruginosa*, bronchiectasis, thin section CT scanning.

Infection of the airways by *Pseudomonas aeruginosa* occurs commonly in patients with cystic fibrosis but also occurs in patients with other forms of bronchiectasis. Although much of the morbidity and mortality of patients with bronchiectasis may be due to chronic infection with *P. aeruginosa*, chronic infection of the airways with this pathogen in patients with cystic fibrosis can be prevented by early institution of anti-pseudomonas chemotherapy. Experiments in vitro have suggested that *P. aeruginosa* plays an important part in the progression of bronchiectasis and mucociliary clearance measurements and results in an experimental model of bronchiectasis in vitro are consistent with this. Computed tomographic (CT) scanning is an accurate and non-invasive method of imaging the bronchial tree and is the technique of choice for the diagnosis of bronchiectasis.

Nagaki et al investigated a group of non-smoking patients with a clinical diagnosis of chronic bronchitis whose airways had been infected by *P. aeruginosa* for at least one year. They found that such patients had significantly more severe bronchiectasis on CT scanning than non-infected matched patients and asymptomatic controls. Similar results were obtained in a study performed at our institution in which patients infected with *P. aeruginosa* appeared to have more extensive bronchiectasis on CT scanning and more severe airflow obstruction than non-infected patients, independent of their smoking history. However, in both these studies the assessment of bronchiectasis on the CT scan was limited.

In this study we have examined in more detail the relationship between infection of the airways by *P. aeruginosa* and the morphological pattern of bronchiectasis on thin section CT scans, and any relation between these and the severity and duration of symptoms, patients’ smoking habits, and respiratory function.

**Methods**

Consecutive adult patients undergoing investigation for known or suspected bronchiectasis between January 1991 and March 1993 were studied, provided that bronchiectasis was present on thin section CT scanning and either mucoid or non-mucoid strains of *P. aeruginosa* were cultured from sputum within three months of the scan. Exclusion criteria were (1) an abnormal sweat sodium concentration (tested in all patients), (2) a history of lobectomy or pneumonectomy (since this would affect the forced expiratory volume in one second [FEV1] and alter the CT scores), and (3) age below 16 years. The control group consisted of randomly selected patients with chronic purulent sputum production and bronchiectasis on CT scanning who were not infected by *P. aeruginosa*. Twenty two patients infected with *P. aeruginosa* and 45 controls were accepted for publication.
Effects of airway infection by Pseudomonas aeruginosa on the CT scans was determined according to the criteria described by Naidich. The CT scoring system used was that described by Reiff et al which has good interobserver agreement. The extent of bronchiectasis, severity of bronchial wall thickening, and severity of bronchial wall dilatation were recorded for each lobe using a four point scoring system (0–3): grade 0 = no bronchiectasis, normal bronchial wall thickness, or no bronchial wall dilatation; grade 1 = bronchiectasis present in none or one bronchopulmonary segment, bronchial wall thickening equivalent to half the diameter of the adjacent vessel, or bronchial wall dilatation equivalent to less than twice the diameter of the adjacent vessel; grade 2 = bronchiectasis present in more than one bronchopulmonary segment, bronchial wall thickening equivalent to 0.5–1 × diameter of the adjacent vessel or bronchial wall dilatation equivalent to 2–3 × diameter of the adjacent vessel; grade 3 = gross cystic bronchiectasis present, bronchial wall thickening equivalent to more than the diameter of the adjacent vessel, or bronchial wall dilatation present equivalent to more than three times the diameter of the adjacent vessel. The total score for each of these parameters was obtained by adding together the scores for the six lobes.

The predominant pattern of bronchiectasis present in each lobe as classified by Reid (cylindrical, varicose or cystic) was recorded. The presence of either small centrilobular plugs or large plugs (plugging of the segmental and subsegmental airways) was recorded as present or absent. To assess involvement of the bronchioles by the disease process areas of decreased attenuation of the lung parenchyma

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**Table 1** Comparison of the demographic and clinical features obtained from the case records in patients with sputum infected with Pseudomonas aeruginosa (Pa + ve group) and those not infected (Pa – ve).

<table>
<thead>
<tr>
<th></th>
<th>Pa + ve group (n = 22)</th>
<th>Pa – ve group (n = 45)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.1 (14.5)</td>
<td>43.5 (14.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>10:12</td>
<td>16:29</td>
<td>0.44</td>
</tr>
<tr>
<td>No. of smokers (ever vs never)</td>
<td>9</td>
<td>16</td>
<td>0.67</td>
</tr>
<tr>
<td>Median (range) history (pack years)</td>
<td>0 (0–40)</td>
<td>0 (0–90)</td>
<td>0.46</td>
</tr>
<tr>
<td>No. with history of asthma</td>
<td>12</td>
<td>18</td>
<td>0.26</td>
</tr>
<tr>
<td>Age at onset of sputum production (years)</td>
<td>27.0 (22.0)</td>
<td>21.2 (18.3)</td>
<td>0.26</td>
</tr>
<tr>
<td>Duration of sputum production (years)</td>
<td>27.1 (14.6)</td>
<td>22.3 (17.4)</td>
<td>0.27</td>
</tr>
<tr>
<td>FEV₁ (% pred)</td>
<td>58.2 (30.1)</td>
<td>75.4 (22.9)</td>
<td>&lt;0.02</td>
</tr>
</tbody>
</table>

FEV₁ = forced expiratory volume in one second. Values are mean (SD) or median (range).

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Figure 1 Thin section slices of a CT scan taken at two similar levels from two patients with bronchiectasis, both with a 29 year duration of sputum production. Sections (a) and (b) are through the upper zones and (c) and (d) are through the lower zones. Sections (a) and (c) are from a patient not infected with P aeruginosa and (b) and (d) are from a patient infected with P aeruginosa.
Global decreased attenuation 0.05 (0.00 to 0.09) 2.5 (0.8 to 4.2)
Bronchial wall thickness 0.02
Centrolobular plug score

Statistical analysis performed by Wilcoxon’s rank sum test.

Results were expressed as medians with ranges. A p value of <0.05 was regarded as statistically significant. Group comparisons were made using the Student’s t test, χ² statistics, or Wilcoxon’s rank sum test. Agreement between observers was expressed as the kappa coefficient; kappa values of >0.60 were taken to indicate good agreement between observers. Correlations were examined by multiple linear regression or, when appropriate, by logistic regression (Stata Data Analysis, Computing Resonance Center, Santa Monica, California, USA).

Table 2 Median scores (with ranges) for morphological features on CT scans in patients with sputum infected with Pseudomonas aeruginosa (Pa +ve) and those not infected (Pa –ve).

<table>
<thead>
<tr>
<th>Morphological Feature</th>
<th>Pa +ve group (n=22)</th>
<th>Pa –ve group (n=45)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extent of bronchiectasis</td>
<td>9.5 (3.5–14.0)</td>
<td>5.0 (1.5–15.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Bronchial wall dilation</td>
<td>9.5 (2.5–17.5)</td>
<td>4.0 (1.0–17.5)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Bronchial wall thickening</td>
<td>6.0 (2.5–12)</td>
<td>3.5 (0–17.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Global decreased attenuation</td>
<td>5.5 (0–12)</td>
<td>2.0 (0–11)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Large plug score</td>
<td>0.5 (0–2.5)</td>
<td>0 (0–2.5)</td>
<td>0.07</td>
</tr>
<tr>
<td>Centrolobular plug score</td>
<td>0.5 (0–5)</td>
<td>0 (0–5)</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Discussion

We have shown that patients who persistently expectorate sputum infected with Pseudomonas aeruginosa have more extensive and severe bronchiectasis on thin section CT scanning than patients whose sputum is not infected with Pseudomonas aeruginosa. The global decreased attenuation score in these...
patients was also significantly greater and related to the duration of sputum production. *P. aeruginosa* produces several virulence factors which are thought to result in the disorganisation of epithelial cells, loss of cilia, and mitochondrial damage that has been observed in vitro when intact respiratory mucosa is exposed to this pathogen.4,20-22 *P aeruginosa* preferentially adheres to mucus and damaged epithelial cells rather than to cilia or uniliated cells.4 In patients with bronchiectasis and cystic fibrosis in whom the mucus is poorly cleared *P aeruginosa* may persist for longer in the airways secrections and produce toxins which stimulate a vicious circle of chronic inflammatory damage to the mucosa, disrupting the normal host defence mechanisms and encouraging persistence of infection.4 This hypothesis may explain why in our study patients infected with *P aeruginosa* had significantly more extensive and severe bronchiectasis, bronchial wall dilatation and thickening with a higher prevalence of cystic and varicose patterns present than non-infected patients, this relationship being preserved even after adjustment for the duration of sputum production. Various hypotheses have been proposed for the mechanism of airway damage in bronchiectasis. Elastase detected in high levels in the sputum of patients with bronchiectasis23 impairs ciliary function and damages bronchial epithelium;4 its presence in sputum has been shown to be associated with gas trapping.24 *P aeruginosa* produces its own elastase24-27 and this may further exacerbate airway damage. Areas of decreased attenuation attributable to obliteration of the small airways are commonly observed in patients with a history of chronic purulent sputum production and bronchiectasis on HRCT scanning,28 suggesting that disease of the small airways may play an important part in the pathogenesis of bronchiectasis. Our study confirms that areas of decreased attenuation are a frequent finding in patients with bronchiectasis and patients infected with *P aeruginosa* achieve a higher global decreased attenuation score than the non-infected patients, indicating a greater degree of small airways disease. The decreased attenuation score in our study was significantly related to the duration of sputum production, suggesting that this feature may be associated with the process of mucus production as demonstrated by in vitro and in vivo experiments.26-27 However, as there was also a significant negative relationship between the presence of centrilobular mucus plugging and the duration of sputum production, it is possible that centrilobular mucus plugging is indicative of inflammation early in the course of bronchiectasis which tends to regress as the bronchiectasis becomes more established when damage to the small airways by an obliterator bronchiolitis becomes the more dominant feature.

This study clearly shows that patients with bronchiectasis infected by *P aeruginosa* have a more extensive and severe spectrum of disease present on HRCT scanning than non-infected patients and the single feature on the CT scan that predicted the likelihood of sputum infection by *P aeruginosa* was increasing thickness of the bronchial wall. Undoubtedly, many complex mechanisms involving the numerous virulence factors produced by *P aeruginosa* are involved throughout the disease process resulting in damage to bronchi and bronchioles but, at present, these in vivo mechanisms are incompletely understood; whether *P aeruginosa* preferentially infects the airways of those patients with more severe bronchiectasis at birth or whether the greater severity of bronchiectasis detected by HRCT scanning is the end result of infection by this organism has not been answered by this study. A reduction in sputum infection by *P aeruginosa* has been associated with an improvement in lung function in cystic fibrosis,4,9 but it remains to be determined whether a significant improvement in morbidity can be achieved in patients with other forms of bronchiectasis who are chronically infected by this pathogen (although preliminary results appear encouraging19).
Effects of airway infection by Pseudomonas aeruginosa: a computed tomographic study.

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