Composition of bronchopulmonary secretions from patients with bronchiectasis

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ABSTRACT Pulmonary function tests were carried out on 17 patients with bronchiectasis and six indices were selected to grade severity. Average concentrations of nine plasma proteins were determined by quantitative immunoelectrophoresis in specimens of sputum and serum from each patient. Wide patient-to-patient variation in concentration was encountered which appeared to follow a continuous progression unrelated to clinical severity. Patients at the upper end of the scale appeared to be responding by exudation and a pulmonary hypersensitivity reaction may be occurring in their lungs. There was evidence of selective concentration in sputum of α1-antichymotrypsin and IgA although IgA concentrations were lower than would be expected in patients with chronic bronchitis. It is suggested that sputum IgA levels could be explored as a diagnostic criterion in those patients who could equally be suffering from chronic bronchitis.

Bronchiectasis is a histopathological description of an alteration in the architecture of the bronchi and the development of symptoms is related to the onset of infection. Before the advent of antibiotic therapy, patients with bronchiectasis tended to produce copious quantities of foul and foetid sputum. However, improvements in oral hygiene and the ready availability of antimicrobial drugs has changed this picture. Symptoms of dyspnoea and wheeze are frequent in bronchiectasis and have been related to the development of chronic bronchitis.

The composition of the ground substance of the sputum has been found by us to be related to the diagnosis in some chest diseases. In the present investigation we examined the soluble proteins of sputum specimens from a series of patients with clinically proven bronchiectasis to see whether the composition of the sol or continuous phase of sputum can be a guide to the existence of bronchiectasis or the development of chronic bronchitis, or if it can be related to the severity of the disease.

Methods

Seventeen patients (nine women and eight men, average age 45±12 years) with a clinical diagnosis of bronchiectasis were admitted to Sully Hospital for investigation.

A clinical questionnaire was completed on all patients noting age of onset of symptoms, cough frequency and nature of sputum, haemoptysis, dyspnoea, and systemic symptoms such as weight loss and malaise. A past history of severe respiratory infection in early childhood was noted specifically and the patient’s smoking habits were documented. Clinical examination by a single observer evaluated the presence or absence of clubbing, cyanosis, anaemia, pulmonary crackles, and right ventricular hypertrophy. Bronchograms had been carried out on 14 of the patients; the remaining three had radiographic changes compatible with bronchiectasis. Radiographic classification was performed by the method of Simon, and the severity assessed on the basis of the number of lobes involved; all films were assessed by one observer.

The forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) were measured with an eight litre McDermott spirometer. All values were compared to the predicted normal values of Cotes.

A 24-hour collection of sputum was carried out on each of the patients. All specimens were processed immediately after collection and weighed aliquots of sputum were centrifuged at 120 000 g (average rotor radius=8·5 cm) using the SW50 rotor in a model L2 spino ultracentrifuge (Beckman Instruments, California, USA) for
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three and a half hours at 4°C. Quantitative
immunoelectrophoresis of the soluble proteins in
the sputum sol phase was carried out substantially
by the same methods as those described in detail
elsewhere.4 The concentration of the plasma
proteins in the specimens of serum from each
patient was measured by the techniques employed
for determining the concentration of the cor-
responding proteins in the sol phase of sputum.

Results

CLINICAL ASSESSMENT

Patients were graded on a simple score on the
basis of six indices chosen because they appeared
to provide the best basis of discrimination
between the individual patients studied. The
indices were: the onset of symptoms before the
age of 5 years; the presence or absence of
dyspnoea when walking quietly on level ground;
the presence of pulmonary crackles; the radi-
ological involvement of four or more lobes (for
this purpose the lingula was considered as a
separate lobe); the presence of airways obstruc-
tion, (FEV1/FEV ratio less than 60%) and a
history of cigarette smoking. The results of the
clinical grading are summarised in table 1. It can
be seen that 10 of the patients had relatively
mild bronchiectasis (grades 0, 1, or 2) and the
remainder had moderately severe or severe
bronchiectasis (grades 3, 4, or 5).

IMMUNOCHEMISTRY

Wide variation was encountered when the con-
centrations of plasma proteins in the sol phase of
sputum were measured (table 2). Patient-to-

patient variation in sputum sol phase albumin
concentrations appeared to follow a progressive
type of pattern that was unrelated to clinical
grading (fig 1). All other plasma protein concen-
trations, with the exception of IgA (r=0·46,
0·05<p<0·1) showed significant correlation with
the sputum sol phase albumin concentrations. The
concentration ratios of albumin in matched
specimens of serum and sputum were inversely
related to the sputum sol phase albumin concen-
trations (r=0·95, p<0·0001), and all other
protein concentration ratios correlated signifi-
cantly with the albumin concentration ratio
except IgA (r=0·29), α1-antichymotrypsin (r=
0·24), and C3 (r=0·25); the probabilities in each
case were 0·2 <p <0·5. The mean concentra-
tions of IgA relative to transferin matched
pairs of sputum and serum were 9·51 ± 6·03 and
1·49 ± 0·63 (t=5·29, <0·0001) and those of α1-
antichymotrypsin in sputum and serum were
4·45 ± 3·19 and 1·73 ± 1·42 (t=3·11; 0·0001 <p
<0·0005) thus suggesting selective concentration
in sputum of these two plasma proteins. In
contrast, the corresponding relative concentra-
tions of C3 in sputum and serum were 3·52 ±
1·43 and 2·37 ± 0·78 and these differences only
just achieved significance (0·025<p<0·05).

Discussion

The patient-to-patient variation in the con-
centrations of the plasma proteins in the sol phase
of the sputum specimens seemed to follow a
continuous progression. Although some patients
appear to produce sputum resembling that of
patients with chronic bronchitis, others at the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Clinical grading of patients with bronchiectasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient number</td>
<td>Indices</td>
</tr>
<tr>
<td>Onset of symptoms</td>
<td>Dyspnoea</td>
</tr>
<tr>
<td>at age 5 years</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
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<td>17</td>
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</table>

NT—not tested

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Table 2  Average concentrations of nine plasma proteins in the sol phase of sputum and in matched serum specimens from 17 patients with bronchiectasis

<table>
<thead>
<tr>
<th>Plasma proteins</th>
<th>Serum concentration (mg/100 ml)</th>
<th>Sputum concentration (mg/100 ml sol phase)</th>
<th>Protein concentration ratios: serum/sputum</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average limits of determined values</td>
<td>Average limits of determined values</td>
<td>Average limits of calculated values</td>
</tr>
<tr>
<td>Albumin</td>
<td>4536 3000-6250</td>
<td>87.5 12-320</td>
<td>122 335-13</td>
</tr>
<tr>
<td>Transferin</td>
<td>229 140-410</td>
<td>6.5 1-2-15-6</td>
<td>68 160-15</td>
</tr>
<tr>
<td>α1-acid glycoprotein</td>
<td>179 62-420</td>
<td>2-5 0-3-5-6</td>
<td>121 309-20</td>
</tr>
<tr>
<td>Haptoglobin</td>
<td>343 124-690</td>
<td>4-7 0-3-17-5</td>
<td>284 783-23</td>
</tr>
<tr>
<td>α1-antitrypsin</td>
<td>224 110-560</td>
<td>13-5 0-7-48-0</td>
<td>60 188-5-5</td>
</tr>
<tr>
<td>α1-antichymotrypsin</td>
<td>36 10-98</td>
<td>2-5 0-2-10-0</td>
<td>26 150-5-5</td>
</tr>
<tr>
<td>B2-globulin (C3)</td>
<td>52 30-75</td>
<td>2-3 0-6-5-6</td>
<td>40 75-8-9</td>
</tr>
<tr>
<td>IgA</td>
<td>337 170-840</td>
<td>42-7 6-5-95</td>
<td>13 29-3-6</td>
</tr>
<tr>
<td>IgG</td>
<td>1416 470-2277</td>
<td>35-3 5-4-91</td>
<td>78 380-3-4</td>
</tr>
</tbody>
</table>

Figure  Variation in sputum sol phase albumin concentrations in individual bronchiectasis patients whose clinical grading has been determined, compared with serum:sputum albumin concentration ratios showing inverse correlation of the values. The IgA concentration ratios in matched serum:sputum specimens are also illustrated to show lack of correlation with the corresponding albumin concentration ratios. ■= Sol phase albumin concentrations, ★= serum:sputum albumin concentration ratios, □= serum:sputum IgA concentration ratios.

upper end of the “scale” have high plasma protein concentrations in the sol phase of their sputum, which is similar to that of patients with status asthmaticus. It is thus possible that a pulmonary hypersensitivity reaction, in the broadest sense of the term, may cause the exudative character of the sputum in a proportion of patients with bronchiectasis. It is of interest that our similar findings in patients with cystic fibrosis could have been caused by the lung damage that characterises this disease and which amounts virtually to bronchiectasis.

Forty per cent of the patients in this study suffered severe bronchiectasis as defined by the indices we describe, but the pulmonary function tests were entirely unrelated to the sputum immunochemistry. There was some evidence suggesting selective concentration of two plasma
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proteins (α1-antichymotrypsin and IgA) in the sol phase of the patients' sputum and this has been noted by us in other chronic chest diseases. However, the average concentration of IgA in the sputum of patients with bronchiectasis was lower than that of sputum from patients with bronchitis. This finding may be worth exploring as a means of providing additional evidence in support of the diagnosis of bronchiectasis in those patients who could equally be suffering from chronic bronchitis.

References

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