Aetiology in adult patients with bronchiectasis

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KEYWORDS
Allergic bronchopulmonary aspergillosis; Bronchiectasis; Immune deficiency; Mycobacteria; Primary ciliary dyskinesia

Summary
Background: Bronchiectasis has a number of causes. Their prevalence is not well documented. The aim of this study was to identify aetiology in a population of patients referred to a specialist clinic with symptoms suggestive of bronchiectasis, to determine the proportion of patients in whom knowing the aetiology altered management. In addition we wished to describe in detail those patients who remained idiopathic to facilitate future studies of this group; and establish the diagnosis in those without bronchiectasis.

Methods: A total of 240 consecutive patients referred to the Royal Brompton Hospital with a history of recurrent chest infections, chronic cough and regular sputum production underwent a 3 day program of investigation.

Results: A total of 165 patients had bronchiectasis on CT scan, an underlying cause was identified in 122 (74%) and this affected management in 61 (37%). The common aetiologies were: post-infection (52), primary ciliary dyskinesia (17), allergic bronchopulmonary aspergillosis (13), and immune deficiency (11). Forty-three patients had idiopathic bronchiectasis. They had symmetrical predominant lower lobe disease with onset of chronic chest and sinus symptoms in middle age.

Conclusion: Full investigation of problematic cases should occur in a specialist centre because results affect management in a third of cases.

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Introduction

Bronchiectasis is defined as abnormal chronic dilatation of one or more bronchi. Patients have a structural abnormality of the bronchial wall that predisposes them to bacterial infection likely due to impaired mucus clearance. A self-perpetuating vicious cycle of chest infections and chronic lung inflammation can lead to further damage of the bronchial wall and spread of disease to normal areas of bystander lung. Symptoms usually include recurrent lower respiratory tract infections, chronic cough and regular sputum production. Chest pains, symptoms of chronic rhinosinusitis and undue breathlessness are also common.

Bronchiectasis has a number of causes, which include: post-infective, e.g. childhood whooping cough or tuberculosis; an insult to the airway of some other kind, e.g. aspiration of gastric contents and smoke inhalation; impairment of the host defences leading to bacterial infections (which may in some cases be hereditary), e.g. primary...
ciliary dyskinesia (PCD) and common variable immune deficiency (CVID); exaggerated immune response, e.g. allergic bronchopulmonary aspergillosis (ABPA) and inflammatory bowel disease; or rarely congenital causes, e.g. Munier–Kuhn syndrome and pulmonary sequestration. In a significant proportion of patients no cause is found. Identifying the cause of bronchiectasis may influence management of the condition. This may relate to therapy, e.g. patients with CVID are given immunoglobulin infusions, and patients with ABPA may benefit from corticosteroids or antifungal agents; or it may relate to other aspects of management, e.g. a diagnosis of PCD will influence decisions about thoracic surgery or choice of middle ear and sinus surgery, and a diagnosis of cystic fibrosis (CF) results in genetic counselling.

Only one previous study has characterised the causes of disease in a large population of adult patients with bronchiectasis, and to date no study has reported on the aetiology of patients who have symptoms suggesting bronchiectasis but no disease on CT scan. Several other papers have included aetiology as a part of a study with wider aims. A significant proportion of patients remain idiopathic after investigation, and the pattern of disease in these patients has not been reported. Full investigation of aetiology, which can only be carried out in a specialist centre, would only be justifiable if the results influenced management in a significant proportion of cases.

**Aim**

The aim of this study was to identify the aetiology in a large cohort of adult patients referred with a history suggesting a diagnosis of bronchiectasis. We were interested in what proportion of patients with a diagnosis of bronchiectasis could be ascribed an aetiology and in what proportion the aetiology influenced management. We wished to contrast the results of patients with idiopathic bronchiectasis who had been fully investigated to those of patients with a post-infective aetiology to see if any patterns emerged.

**Methods**

**Subjects**

A total of 240 consecutive patients were referred to the unit by colleagues in secondary care hospitals and underwent a protocol of investigations, with ethical committee approval, into their chest condition during a 3-day stay in the minimal dependency unit at the Royal Brompton Hospital, London. The study was performed over a 5-year period (1st March 2001–1st March 2006). All patients entering the protocol were new to the hospital and referred because of symptoms suggestive of bronchiectasis. These included in all patient’s regular sputum production, chronic cough and a history of recurrent lower respiratory tract infections. Patients referred during this time for a specific test, e.g. ciliary function or with a specific question about management, e.g. antibiotic treatment of non-tuberculosis mycobacterial infection did not go through this full protocol of investigations and were not included.

**Protocol of investigations**

Patients underwent a pre-programmed protocol of investigations as described below:

**History:** A complete medical history was taken from the patient, including age of onset, chest symptoms, sputum description, sinus and nasal symptoms, previous respiratory illnesses including childhood history, respiratory risk factors, and associated illnesses and conditions. Post-infective bronchiectasis was diagnosed when the patient reported a history of symptoms with onset immediately after a severe infection, such as pneumonia or whooping cough. Where possible relatives were also questioned on childhood illnesses in order to try and obtain an accurate history. Patients with a history of childhood pneumonia, but who then had a prolonged period of no respiratory symptoms were not classified as post-infective. Bronchiectasis associated with inflammatory bowel disease was diagnosed where patients had ulcerative colitis, crohn’s disease or coeliac disease and also developed bronchiectasis (in some cases post-colectomy). Young’s syndrome was diagnosed when there was a history of bronchiectasis, sinusitis and azoosperma in males and/or a history of mercury poisoning or pinks disease in childhood. Yellow nail syndrome was diagnosed when examination showed yellow discolouration of dystrophic nails together with bronchiectasis and sinusitis, whether or not patients had other features of the syndrome.

**Blood investigations:** Serum immunoglobulins (Ig), IgG, IgA, IgM, IgE were measured. From March 2001 to June 2004 IgG subclasses were measured, but latterly specific antibody levels to pneumococcal and tetanus antigens were assessed. If these were low they were repeated 6 weeks after vaccination. Blood investigations also included Aspergillus fumigatus radioallergosorbent (RAST) test and IgG precipitins; serum protein electrophoresis strip and urine electrophoresis; autoantibodies including rheumatoid factor; α1-antitrypsin and phenotype if the level was low. A serum IgE of > 150 IU/ml and aspergillus RAST of > 10 IU/ml together with sputum and/or peripheral blood eosinophilia, and compatible radiology was required to fulfil the diagnosis of ABPA.

**Radiology:** All patients had a digital chest radiograph (PA and lateral), sinus radiograph and high-resolution computed tomography (HRCT) scan. HRCTs were performed on either a 4 or 64-channel multidetector CT machine (Siemens volume zoom; Siemens, Elangen, Germany) using a standard protocol of 1 or 1.5 mm sections at 10 mm intervals. Sections were obtained with the patient in a supine position breath holding at near total lung capacity. Images were reconstructed with a high special resolution algorithm and viewed at appropriate window settings (Level 500, width 1500 Hounsfield Units). Bronchiectasis was diagnosed by standard CT criteria. Patients were classified from their CT scan prior to any knowledge of their other results as, no bronchiectasis, mild (one lobe with bronchiectasis), moderate (two or three lobes with bronchiectasis), or severe (four or more lobes with bronchiectasis or cystic changes in two or more lobes). This classification was determined utilising the radiology report by Dr. R. Wilson and cases in which there was any doubt were discussed with a single radiologist (Prof. David Hansell, Royal Brompton Hospital).
Respiratory function tests: A full set of respiratory function tests including forced expiratory volume (FEV₁) were performed.

Sputum investigations: The following investigations were performed on fresh sputum samples. Microscopy (for cell count of eosinophils), routine culture and antibiotic sensitivities, smear and culture for acid fast bacilli (3 samples on 3 successive days). 16,17

Ciliary function tests: Nasal mucociliary clearance was measured by the saccharin test, 18 and nasal nitric oxide were performed on each patient as screening tests. 19 If these tests were abnormal the patient underwent nasal brush biopsy. Samples were analysed for cilia beat frequency and beat pattern under light microscopy, 20 and cilia ultrastructure was studied by electron microscopy. 21

Investigations for cystic fibrosis: A sweat test was used as a screening test. 22 This was followed by cystic fibrosis genotyping from a blood sample if the sweat test was positive (Na⁺, Cl⁻ > 90 µM/l) or borderline (Na⁺ and Cl⁻ 70–90 µM/l), or other features of the case (e.g. upper lobe bronchiectasis or a family history) suggested the diagnosis.

Additional investigations: If CT scan showed localised bronchiectasis or had unusual features a bronchoscopy was performed. If aspiration was suggested from the history then the patient underwent video fluoroscopy.

Idiopathic bronchiectasis

Patients who did not fulfil the definition of post-infective and with normal or negative results of investigations into the cause of bronchiectasis were classified as idiopathic. The idiopathic group were compared to the post-infective group with respect to: age at onset, age at referral, symptoms since onset as chronic or intermittent (symptom-free periods), childhood illnesses (specifically whooping cough, complicated measles, pneumonia and whether or not there was a history of wheeziness), presence of chronic rhinosinusitis, number of bronchiectatic lobes and distribution of disease (whether bilateral, predominantly lower, middle or upper lobe), smoking history and history of surgery.

Statistical analysis

Groups were compared using an ANOVA or Mann–Whitney test where data was ordinal, and a χ² test of independence or Fisher exact test for nominal data. The appropriate test was chosen according to group size and distribution. A p-value of < 0.05 was considered statistically significant.

Results

Bronchiectasis was present on CT scan and considered to be the pathology accounting for the chest symptoms of 165 patients. The aetiologies determined by the investigations are shown in Table 1. The average age of patients was 49 yr range 17–87. Patients with conditions present since birth (PCD n = 17 and CF n = 2) and primary immune deficiency n = 7 mean age (SD) 39 yr (14) were younger than patients with idiopathic n = 43 51 yr (14), post-infective n = 52 49 yr (16) and all other causes of bronchiectasis n = 44 54 yr (16) (p<0.01). An aetiology was found in 122 of the 165 patients with bronchiectasis (74%). The cause was thought to affect future management of the patients in 61 cases (37%). These were: PCD, ABPA, immune deficiency, ulcerative colitis, pan bronchiolitis, mycobacterium infection, rheumatoid arthritis, aspiration, CF. The majority of patients were female (65%) which was true for all aetiologies except Young’s syndrome, pan bronchiolitis, yellow nail syndrome, aspiration and CF.

Allergic bronchopulmonary aspergillosis (n = 13)

Total serum IgE was mean (SD) 2653.8 IU/ml (3806.4) The A. fumigatus RAST in this group was mean 29.8 IU/ml (SD = 28.1) range 0.34–101 IU/ml. One patient had A. fumigatus RAST within the normal range (<0.35)

<table>
<thead>
<tr>
<th>Cause</th>
<th>n (% of study population)</th>
<th>Age (SD)</th>
<th>No. males (% group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post infection</td>
<td>52 (32)</td>
<td>49 (16)</td>
<td>17 (33)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>43 (26)</td>
<td>51 (14)</td>
<td>15 (35)</td>
</tr>
<tr>
<td>PCD</td>
<td>17 (10)</td>
<td>36 (13)</td>
<td>5 (29)</td>
</tr>
<tr>
<td>ABPA</td>
<td>13 (8)</td>
<td>54 (13)</td>
<td>6 (46)</td>
</tr>
<tr>
<td>Immune deficiency</td>
<td>11 (7)</td>
<td>47 (18)</td>
<td>1 (9)</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>5 (3)</td>
<td>48 (20)</td>
<td>2 (40)</td>
</tr>
<tr>
<td>Young’s syndrome</td>
<td>5 (3)</td>
<td>56 (5)</td>
<td>3 (60)</td>
</tr>
<tr>
<td>Pan bronchiolitis</td>
<td>4 (2)</td>
<td>46 (21)</td>
<td>3 (75)</td>
</tr>
<tr>
<td>Yellow nail syndrome</td>
<td>4 (2)</td>
<td>55 (14)</td>
<td>2 (50)</td>
</tr>
<tr>
<td>Mycobacterium infection</td>
<td>4 (2)</td>
<td>62 (20)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>3 (2)</td>
<td>65 (4)</td>
<td>1 (33)</td>
</tr>
<tr>
<td>Aspiration</td>
<td>2 (1)</td>
<td>67 (13)</td>
<td>1 (50)</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>2 (1)</td>
<td>41 (13)</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>165</td>
<td>49 (16)</td>
<td>58 (35)</td>
</tr>
</tbody>
</table>

ABPA = allergic bronchopulmonary aspergillosis.
PCD = primary ciliary dyskinesia.
0.34 IU/ml but elevated IgE (702 IU/ml) and positive precipitins to *A. niger* and *A. flavus*. Five other patients in this group had *A. fumigatus* positive precipitins. One patient had IgE within the normal range, ABPA was diagnosed aged 13 years when he presented with left lower lobe pneumonia which was found to be eosinophilic, aspergillus was cultured from the sputum, there was peripheral blood eosinophilia and aspergillus precipitins were positive. When referred to the Brompton Hospital aged 58 his serology was no longer active.

Deficient immune response (*n* = 11)

Seven patients had primary immune deficiency. Four patients had CVID, with pan hypogammaglobulinaemia. Three patients of 89 tested had specific polysaccharide antibody deficiency to pneumococcal antigen (SPAD). These patients had normal response to tetanus. Four patients had a secondary immune deficiency due to Hodgkins lymphoma (2) multiple myeloma (1) and chronic lymphatic leukaemia (1).

Abnormal mucociliary clearance (*n* = 24)

**Primary ciliary dyskinesia** (*n* = 17): Twelve patients had a definite ultrastructural defect of their cilia. These were: absence of both dynein arms (5), outer dynein arm defect (4), inner dynein arm and radial spoke defect (2), transposition defect (1). Five patients were classified as probable PCD on the basis of suggestive history, abnormal screening tests, abnormal ciliary beat frequency or pattern but inconclusive electron microscopy due to the inadequate size of the sample obtained by brush biopsy. All 17 patients had a low nasal nitric oxide of <100 ppb mean (SD) 34.5 ppb (23.4). In patients with moving cilia the average ciliary beat frequency was low *n* = 10, 9.1 Hz (3.6) (normal range 11–16 Hz). In 7 patients the cilia were completely static (0 Hz). Ciliary beat pattern was reported as stiff (6), slow (4), dyskinetic (3) and normal (1). More than one description was used per sample. Five patients in this group had complete situs inversus and one patient had dextrocardia alone.

**Cystic fibrosis** (*n* = 2): Genotyping showed a Delta F508 homozygous in one case and Delta F508/711+3AG mutation in the other.

**Young’s syndrome** (*n* = 5): All five patients had bronchiectasis and sinusitis on CT. Three males had obstructive azospermia. The two females had a history of pinks disease as babies and a subsequent diagnosis of bronchiectasis as teenagers (15 and 17 yr).

**Mycobacterium infection** (*n* = 4)

Two patients had bronchiectasis post tuberculosis. In two cases bronchiectasis was thought to be due to primary infection with *Mycobacterium avium* complex because of the history and HRCT scan appearance. 23

**Inflammatory bowel disease** (*n* = 5)

These patients all had ulcerative colitis. Three patients had ulcerative colitis diagnosed whilst young (aged 13–24) followed by colectomy (aged 23–35). Chest symptoms began in two patients 6 months after surgery, the third began producing regular sputum 10 years prior to colectomy when her ulcerative colitis was poorly controlled. The other two patients did not have surgery. One had an ICU admission after being born prematurely, but was then well until developing ulcerative colitis and a productive cough in her teens. The other was diagnosed with ulcerative colitis in her 50 s, and developed diffuse bilateral bronchiectasis aged 65 with no other aetiological factor identified.

**Yellow nail syndrome** (*n* = 4)

There was evidence of yellow discoulouration of dystrophic nails and bronchiectasis in all four patients. 14 in all patients onset of nail and chest symptoms was simultaneous. All had sinusitis and two had peripheral lymphoedema. There were no other features of the syndrome. Three showed improvement of their nails as control of chest symptoms improved. One patient had no nail improvement despite improvement in the chest.

**Rheumatoid disease** (*n* = 3)

In one patient chest symptoms developed aged 47 coinciding with symptoms of rheumatoid arthritis. Rheumatoid factor was 1 in 80. The second patient had a chest history dating back to age 10 which worsened with the onset of acute rheumatoid arthritis aged 34 requiring gold injections. Rheumatoid factor was 1 in 160. The third patient had Sjogren’s syndrome, and cough and sputum production which began aged 35. This got progressively worse requiring a first hospital admission for iv antibiotics age 54. Rheumatoid arthritis was diagnosed age 53. Rheumatoid factor was 1 in 640.

**Aspiration of gastric contents** (*n* = 2)

One patient had severe gastro-oesophageal reflux and Barrett’s oesophagus. The second had a dilated oesophagus. Aspiration was strongly suspected from the history in both cases but could not be confirmed by video fluoroscopy.

**Pan bronchiolitis** (*n* = 4)

These four patients had widespread mild to moderate airway dilatation with bilateral diffuse "tree-in-bud" appearance on CT scan. They suffered from dyspnoea and a productive cough. Two patients had a bronchoscopy showing inflammation of the bronchial mucosa and biopsy which showed infiltration with plasma cells, lymphocytes and foamy cells. All four patients responded well to a prolonged course of azithromycin.

**Post-infection** (*n* = 52)

Average age of onset of symptoms in these patients was 7 years (SD = 11) and the average age of referral to Brompton was 49 yr (16). They were predominantly female (67%). One third had a smoking history. Half suffered from
Table 2  Comparison of characteristics of patients with idiopathic bronchiectasis and patients with bronchiectasis post infection.

<table>
<thead>
<tr>
<th></th>
<th>Idiopathic group</th>
<th>Post-infection group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>43</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Gender No. males (%)</td>
<td>15 (35)</td>
<td>17 (33)</td>
<td>ns</td>
</tr>
<tr>
<td>Age at onset (SD)</td>
<td>43 (15)</td>
<td>49 (16)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age at referral to Royal</td>
<td>51 (14)</td>
<td>49 (16)</td>
<td>ns</td>
</tr>
<tr>
<td>Brompton Hospital (SD)</td>
<td>4.1 (1.7)</td>
<td>4.3 (1.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Mean number of lobes</td>
<td>41 (95)</td>
<td>49 (94)</td>
<td>ns</td>
</tr>
<tr>
<td>Involved (%)</td>
<td>32 (74)</td>
<td>24 (46)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Predominantly lower lobe</td>
<td>36 (84)</td>
<td>26 (50)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Bronchiectasis (%)</td>
<td>36 (84)</td>
<td>26 (50)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Chronic rhinosinusitis</td>
<td>11 (26)</td>
<td>11 (21)</td>
<td>ns</td>
</tr>
<tr>
<td>Wheezy bronchitis in</td>
<td>14 (33)</td>
<td>17 (33)</td>
<td>ns</td>
</tr>
<tr>
<td>childhood (%)</td>
<td>36 (84)</td>
<td>25 (48)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Smoking history (%)</td>
<td>13 (30)</td>
<td>17 (33)</td>
<td>ns</td>
</tr>
<tr>
<td>Lobectomy (%)</td>
<td>1 (2)</td>
<td>5 (10)</td>
<td>ns</td>
</tr>
</tbody>
</table>

Chronic rhinosinusitis. The majority (94%) had bilateral bronchiectasis, the lower lobes were the worse affected in half the patients. Wheezy bronchitis in childhood was described by a minority of patients (21%). Forty-seven patients developed bronchiectasis following a childhood infection. These infections were unspecified pneumonia (28), whooping cough (16), and complicated measles (3). Five patients developed bronchiectasis following an infection in adulthood. Five patients had received lung surgery for their bronchiectasis. Table 2 shows the characteristics of these patients compared with the idiopathic group.

**Idiopathic bronchiectasis (n = 43)**

Average age of onset of symptoms in these patients was 43 years (SD = 15) and the average age of referral to Royal Brompton Hospital was 51 yr (14) (Table 2). They were predominantly female (65%). Almost all suffered from chronic rhinosinusitis. One-third (30%) had a smoking history (mean 11 pack years). This was similar to the group in whom aetiology was diagnosed (30%). The majority (84%) described their symptoms as chronic since onset and only a small proportion (14%) described an acute viral like illness at onset of their symptoms. Wheezy bronchitis in childhood was described by a minority of patients (26%). A quarter (n = 10) did describe childhood pneumonia, but then suffered no further respiratory symptoms until middle age. The group as a whole had predominantly symmetrical lower lobe bilateral bronchiectasis but the 10 patients who gave a history of childhood pneumonia had more widespread disease particularly involving the middle lobes in 5 of 10 cases, whereas in only 2 of the remaining 33 cases was the disease not predominantly lower lobe (p <0.005). The group with a past history of childhood pneumonia was otherwise identical to the rest of the idiopathic group.

Table 2 shows a comparison between the idiopathic and post infective groups. The significant differences were: age of onset; distribution of bronchiectasis; presence of chronic rhinosinusitis and whether the onset of symptoms was intermittent or chronic. The majority of the idiopathic group had lower lobe bronchiectasis whereas in the post-infective group it was more variable. Nearly 84% of the idiopathic patients described chronic rhinosinusitis compared to only 50% in the post-infection group. In the idiopathic group the majority (84%) described their symptoms as chronic since onset, whereas in the post-infection group in 52% of patients symptoms started off as intermittent.

**Bacteriology and lung function**

A total of 59% of patients had a positive sputum culture at the time of their assessment. In PCD a much larger proportion of patients had positive bacteriology (94%) than in other groups. None of the five patients with ulcerative colitis had positive sputum cultures. Chi-squared test of independence showed no significant difference between incidence of bacterial infection between different aetiologies (p>0.05). *Pseudomonas aeruginosa* was present in the sputum of 22% of the patients. There was no significant difference between lung function or disease severity on CT scan between different aetiologies of bronchiectasis p>0.05. FEV1 was mean (SD) 72% (24) predicted. There was a significant relationship between CT severity score and lung function (FEV1% predicted) compared by ANOVA, mild n = 27 mean (SD) = 84.6 (24.5), moderate n = 75 76.0 (24.7), severe n = 63 60.2 (21.3) p<0.0001. Patients with *P. aeruginosa* infection had significantly reduced FEV1% predicted n = 36 mean (SD) = 60.5 (20.6) compared to infection with other bacteria n = 62 mean (SD) = 72.0 (25.8) or no bacteria cultured from the sputum sample n = 67 mean = 76.2 (25.2) (p<0.05).

**Other patients**

In the remaining 75 patients, 54 had no bronchiectasis on HRCT scan. The cause of these patients symptoms were: asthma (24), mucus hypersecretion (7), emphysema (3), chronic sinusitis without lung disease (3), smoking-related chronic bronchitis (2), eosinophilic bronchitis (2), recurrent pneumonias due to aspiration (1), scarring due to previous *Mycobacterium tuberculosis* infection (1), ulcerative colitis (1), chronic lymphatic leukaemia (1), obliterative bronchiolitis and interstitial lung disease (1), bronchial
Discussion

Investigation of 240 patients presenting with chronic cough, regular sputum production and recurrent chest infections, revealed 165 to have bronchiectasis as their predominant pathology on CT scan. A cause or association of bronchiectasis was identified in 122 (74%) of these patients. This affected management in 37%. The cases referred to our tertiary care unit are likely to be more complex than those seen in a less specialist hospital and are usually referred because of poor control of symptoms or progressive disease. This selection process is likely to have influenced the outcome of our study and aetiologies with more stable disease, such as localised bronchiectasis following pneumonia would likely represent a greater proportion in an unselected population. Full investigation may not be required in all cases of bronchiectasis, but we suggest that the results of this study are applicable in patient’s where their condition is causing concern and in these patients full investigation into their disease should occur. In most countries this would involve referral to a specialist centre such as our own. Ascertaining the aetiology of bronchiectasis may also allow more accurate assessment of the benefits of treatments that may vary in their efficacy in different groups.

A breakdown of aetiology within bronchiectasis patients has only been studied once previously. In a study of 150 patients Pasteur et al. found that investigations similar to those performed in the present study identified a cause in 93 cases: post-infection (44), immunological defect (12), ABPA (11), aspiration/reflux (6), Young’s syndrome (5), CF (4), rheumatoid arthritis (4), PCD (3), ulcerative colitis (2), pan bronchiolitis (1) and congenital (1). Broadly speaking our results are similar to those of Pasteur et al. The greater prevalence of patients with PCD may have occurred because our hospital is a specialist centre for the diagnosis of PCD, but we feel that this is unlikely to be the explanation because patients referred for ciliary function assessment because this was the suspected diagnosis were not included in the analysis. This suggests that the prevalence of PCD is greater than previously reported. The finding that ABPA was the cause of bronchiectasis in 8% in the present study is in keeping with estimations of ABPA as a cause of bronchiectasis in 10% of cases.

Our finding of an immunodeficiency as a cause of bronchiectasis was similar to the study of Pasteur et al. The distribution of IgG subclasses in the serum of healthy adults is skewed, and severe or even complete absence of a subclass has been found in healthy controls. This has lead to a change in our investigation protocol and a reclassification of patients previously diagnosed as having subclass deficiency if their pneumococcal responses were normal. Only three cases in our study failed to generate an antibody response to polysaccharide antigen, which has recently been suggested to account for a much larger proportion of cases. This does not support the idea that this form of immune deficiency accounts for a significant proportion of idiopathic cases which had been missed because total antibody levels were normal.

In both studies there are a large proportion of bronchiectasis cases caused by childhood infection. In the present study infection made up 32% of the cases and 44% in the Pasteur study. We have defined post-infective bronchiectasis when the symptoms suggesting bronchiectasis followed directly after a severe infection. This increases the chances of a causal relationship and lessens the influence of patient recall. However, it makes it likely that some of the patients we have classified as idiopathic are in fact post-infective. It is notable that summing idiopathic and post-infective, respectively, in published series produces the same result: 53.29 (82%), 25.65 (90%), 81.16 (97%), 36.46 (82%). However the total (idiopathic plus post-infective) in the present study is less (58%) possibly because a population of patients referred because of poor control of symptoms contain less patients with these aetiologies. A recent study of a paediatric population of non-CF bronchiectasis patients shows a marked decrease of post-infective cases, compared to a similar study in the 1960s when most of the patient’s in our study were children. This has been attributed to a decrease in the prevalence of measles, TB and pertussis in the UK since the institution of vaccination programmes and the ready availability of antibiotic therapy. If this trend is true, future studies may document a fall in the proportion of cases with childhood infection as the cause of adult bronchiectasis. Although these cases had symptoms of bronchiectasis from childhood, they were not referred to our specialist centre until middle age when a deterioration in symptom control led to referral. The cause for this deterioration was often unclear. Only three cases had bronchiectasis caused by an infection in adulthood. We believe that these patients may be more straight forward to manage and therefore will not be referred to a specialist centre.

The average age of the study group was 49 years and the group was predominantly female (65%). These findings are similar to those of Pasteur et al. in which the group age was 52 years and 63% female. However, in a similar study of children with bronchiectasis there was an equal sex distribution. The predominance of females was across most aetiologies in our study, and since pathogenesis is so varied, this makes a genetic explanation unlikely. It has been shown that females find symptoms of chronic cough more troublesome than males and therefore are more likely to seek medical attention, which might in part explain the female predominance in our study.

In this study there was no indication that disease severity was directly related to the different aetiologies of bronchiectasis in adults, although there was a relationship between the disease severity markers themselves. Correlations between lung function, severity of disease on HRCT scan and infection with P. aeruginosa have previously been reported in bronchiectasis. In patients with ulcerative
colitis there was no positive bacteriology found, which is in keeping with previous reports of bronchiectasis associated with this condition.8

We have looked closely at the patients who remained idiopathic after completing their investigations. Wheezy bronchitis in childhood or an acute onset involving a ‘viral-like’ illness occurred in a minority of patients. The onset of symptoms occurred in middle age and were usually chronic once they had begun. The group as a whole were found to have symmetrical bilateral predominant lower lobe bronchiectasis, particularly the group with no respiratory history. The patients who gave a history of childhood pneumonia but no further respiratory problems before developing symptoms of bronchiectasis in middle age had more variable distribution of disease particularly involving the middle lobes, as in patients whose respiratory problems followed directly after childhood pneumonia. However this finding should be viewed with caution due to the unreliability of patients’ memory. Otherwise the group was remarkably homogenous, and this might suggest a common abnormality. They also differed from the post-infective group in that they had a higher incidence of upper respiratory tract symptoms and their chest symptoms were chronic from onset, whereas half the post-infective group had intermittent symptoms at onset. A recent study carried out by our group on patients with idiopathic bronchiectasis has suggested genetic abnormality with impaired HLA class I expression and natural killer cell dysfunction,31 and further studies are warranted that might elucidate dysregulation of the inflammatory response.

Where no bronchiectasis is found on HRCT scan some of the causes of symptomology are the same as the causes of bronchiectasis such as PCD, ulcerative colitis, chronic lymphatic leukaemia and alpha-1 antitrypsin deficiency. These patients are at risk of developing bronchiectasis in the future. In most other cases there is another aetiology to explain the symptoms.

In conclusion, following investigation, the aetiology of bronchiectasis can be identified in approximately two-thirds of cases. In 37% of patients knowledge of aetiology affected future management of their condition. Patients with idiopathic bronchiectasis have onset of chronic symptoms in middle age and usually have bilateral predominantly lower lobe disease.

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References


