Bronchiectasis: the Consequence of Late Diagnosis in Chronic Respiratory Symptoms

by Deniz Doğru, Afssane Nik-Ain, Nural Kiper, Ayhan Göçmen, Uğur Özçelik, Ebru Yalçın, *and* Ayşe Tana Aslan
Department of Pediatrics, Pulmonary Medicine Unit, Hacettepe University, Ankara, Turkey

Summary

Bronchiectasis is still common among some developing countries like Turkey. The aim of this study was to document the number of children with non-cystic fibrosis (CF) bronchiectasis, to evaluate the risk factors and to emphasize early diagnosis and treatment. All children, except those diagnosed with CF, with bronchiectasis established by chest radiogram, bronchography and/or computed tomography or biopsy material, were retrospectively reviewed. They were tested for serum total eosinophil count, nasal smear, serum levels of immunoglobulins A, G, M, E, and serum alpha-1 antitrypsin level. Pulmonary function tests, rigid bronchoscopy, nasal biopsy, lung scintigraphy, and echocardiogram were also performed. There were 204 patients whose most common presenting symptoms were cough, sputum expectoration, and dyspnea. Bronchiectasis was present mostly in the left lower lobe. The cause could not be determined in 49 per cent of patients. Among the identified causes, infection was present in most patients, followed by asthma, primary ciliary dyskinesia, congenital immune deficiency, and foreign body aspiration. It is possible to prevent bronchiectasis in children with vaccinations and improved nutrition in developing countries. Early diagnosis and treatment will increase the quality of life and survival of patients with bronchiectasis, which has irreversible and progressive complications if untreated.

Introduction

Bronchiectasis is a progressive condition that causes permanent changes in the structure and function of the airways. It is characterized by frequent bacterial infections and inflammatory destruction of the bronchial and peribronchial tissue.[1] Barker and Bardana[2] referred to bronchiectasis as an 'orphan disease' as it is an uncommon disease that is neglected in research and treatment development. Bronchiectasis is rarely seen in developed countries except in patients with cystic fibrosis (CF), primary ciliary dyskinesia, immune deficiency, or focal pulmonary abnormalities. In contrast, it remains common among some developing countries, such as Turkey.[3,4] In such countries, it is important to recognize the high-risk groups as early treatment, early diagnosis, and effective treatment increase the survival and quality of life of the patients. The aim of this study was to document the number of children with non-CF bronchiectasis diagnosed in our hospital and to evaluate the risk factors that cause bronchiectasis and to emphasize early diagnosis and early treatment.

Correspondence: Deniz Doğru, MD, Department of Pediatrics, Pulmonary Medicine Unit, Hacettepe University, Sıhhiye, Ankara 06100, Turkey.
E-mail <ddogru@hacettepe.edu.tr>.

Materials and Methods

Children diagnosed with bronchiectasis at Hacettepe University Pediatric Pulmonary Medicine Unit in Ankara, Turkey over a period of 13 years were included in the study. The diagnosis of bronchiectasis was established by: clinical history of daily or frequent cough with sputum production for more than 3 months; radiological methods such as chest radiogram compatible with bronchiectasis (saccular changes or cylindrical outlines of airway that widen as airways extend into the periphery) and bronchography and/or computed tomography; and with biopsy material, if obtained. Bronchography was used before 1990 as it was the only radiological method available for the exact diagnosis of bronchiectasis. CF was excluded in all patients with sweat chloride test. All patients had chest radiograms. Serum total eosinophil count, nasal smear, and serum levels of immunoglobulins A, G, M, E were obtained. One hundred and nine patients aged more than 6 years old had pulmonary function tests with spirometry. Rigid bronchoscopy, bronchography, plain sinus graphy, nasal biopsy, lung scintigraphy, and echocardiogram were also performed. The age

doi: 10.1093/tropej/fmi036 Advance Access Published on 12 May 2005

at diagnosis, sex, family history, presenting symptoms, physical examination findings, presence of associated abnormality, and etiologic factor were retrospectively evaluated. 'Infection' was defined as symptoms such as fever, cough and sputum expectoration together with radiological findings consistent with pneumonia.

Results

Among 204 patients diagnosed with bronchiectasis, 99 were females (48.5 per cent) and 105 were males (51.5 per cent). The mean age of all patients was 7.16 ± 3.72 years. The disease was diagnosed mostly at 8 years of age. There was consanguinity of parents in 76 patients (37.2 per cent). The most common presenting symptom was cough (83.3 per cent) followed by sputum expectoration (22.5 per cent) and dyspnea (8.8 per cent).

Failure to thrive was obtained in 94 patients (46.1 per cent) at the time of diagnosis. Body weight was under the third percentile in 55 patients (35 per cent) at follow-up. Furthermore, 18 patients had ottitis media, two had adenoid vegetation, and 10 had loss of hearing at different levels. Other physical examination findings are shown in Fig. 1.

Every patient had a chest radiogram. The diagnosis was made by bronchography and thoracal computed tomography (CT) in seven patients with atelectasis, and nine patients with chronic changes in chest radiograms. The diagnosis of bronchiectasis was confirmed by evaluation of lobectomy material in three patients who had atelectasis. In chest radiograms, bronchiectasis was present mostly in the left lower (148 patients, 72.5 per cent) and right lower lobes (115 patients, 56.4 per cent), followed by the right middle lobe in 25 patients (12.3 per cent), right upper lobe in 10 patients (4.9 per cent), and left upper lobe in 13 patients (6.4 per cent). More than one lobe was involved in 91 (44.6 per cent) of the patients. The most common combination was left lower and right lower lobe in 52 patients. Atelectasis was obtained in 57 (28.2 per cent) and dextrocardia was present in 13 patients. The distribution of lobes involved and types of bronchiectasis obtained in bronchographies is shown in Table 1.

Hypertrophia in maxillary sinuses or loss of aeration in unilateral or bilateral maxillary sinuses was obtained in 108 out of 125 tested patients (84.6 per cent). Bronchoscopy revealed copious mucus secretions in 29 and foreign bodies in seven out of 44 tested patients.

Immune deficiencies were obtained in 11 patients; four patients had ataxia telengiectasia, two had common variable immune deficiency, two had selective IgA deficiency, two had IgG subgroup deficiency, and one had X-linked agammaglobulinemia. Total eosinophil count was more than $400/mm^3$ in 27 patients and eosinophils were detected in 32 patients' nasal secretions. IgE level was more than 300 IU/l in three patients.

Tuberculin skin test with 5 TU was more than 10 mm in 46 patients. This positivity was attributed to BCG vaccination in 24 patients and they were not treated. Twelve patients were treated with isoniasid 5 mg/kg for 9 months because of positivity of tuberculin skin test and 10 patients were treated with antituberculous drugs as they had a history of contact with a tuberculosis (TB) patient, clinical and radiological findings of TB in addition to a positive tuberculin skin test.

Nasal biopsy was taken in 16 patients, which revealed secondary changes due to upper respiratory tract infection and changes in spoke orientation in one patient. Primary ciliary dyskinesia was diagnosed

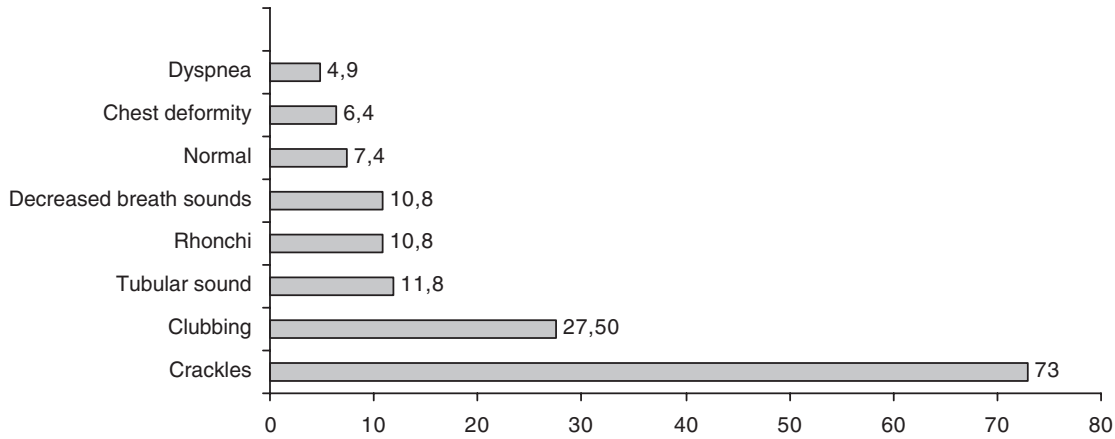

FIG. 1. Physical examination findings of the patients.

TABLE 1
The distribution of lobes and types of bronchiectasis

Lobe	Cylindric	Fusiform	Saccular	Obstructive	Not defined
Right upper		2	3		
Right middle	4	1	4	1	
Right lower	10	11	11		4
Left upper		1	3		
Left lower	16	11	28	2	8
Total	20	26	49	3	12

TABLE 2
Etiological factors for bronchiectasis

	No. of patients	%
Infection	33	16.1
Non-specific	23	
Tuberculosis	10	
Asthma	24	11.8
Primary ciliary dyskinesia	24	11.8
Congenital immune deficiency	11	5.4
Ataxia telengiectasia	4	
Defiency of IgA and IgG2	2	
Defiency of IgA	2	
Common variable immune deficiency	2	
X-linked gammaglobulinemia	1	
Foreign body aspiration	7	3.4
Radiotherapy and chemotherapy	2	1
Sulphur inhalation	1	0.5
Chest deformity	1	0.5
Yellow nail syndrome	1	0.5
Unknown	100	49
Total	204	100

in an additional 23 patients who had dextrocardia and a similar family history.

Pulmonary function tests with spirometry was performed in 109 patients, which showed obstructive and restrictive changes in 61 (55.9 per cent), obstructive in 35 (32.1 per cent), normal in 12 (11 per cent), and restrictive in one (0.9 per cent) patient.

The etiologic factors for bronchiectasis in our patients are shown in Table 2.

Discussion

In this study, the late presenting age of the patients, failure to thrive, digital clubbing, and the predominance of saccular lesions show that our patients presented with advanced and severe disease. When the presenting age of our patients was compared with other reports, we found that our patients presented at an older age than reported in the literature. Most patients are generally reported to present in preschool years.[3–6]

It is known that cylindric dilatation is seen in mild disease and is reversible, but saccular bronchiectasis occurs as the process continues and damage to muscular layers and destruction of elastic tissue, edema and inflammatory cell infiltration into the surrounding tissue occur.[1] Our most common type of bronchiectasis was saccular, which is irreversible and has an unfavorable prognosis.

In our study the most common presenting symptom was cough followed by sputum expectoration, which is in concordance with the literature.[1,3,7] Although hemoptysis is a common symptom in adults,[1] its prevalence was found to be 4–7 per cent in pediatric series.[3,8] In our study, prevalence was 3.9 per cent and was not massive. Although it has been reported that most patients present with infection,[9] the percentage of our patients who presented with fever and severe infection symptoms was 7.8 per cent. In other series, recurrent infection was found in 35 per cent of patients,[3,7] whereas it was only 6.4 per cent in our study.

Bronchiectasis is most commonly seen in the lower lobes, especially in the left lower lobe. The upper lobes are involved less frequently in contrast to CF, probably because of the faciliated mucociliary clearance by gravity.[10] We found that the most common involved lobes were the left lower lobe and the right lower lobe. In the literature, it has been reported that left lower lobe and lingulae were most commonly affected, followed by the right middle lobe and the right lower lobe.[3,6,9] However, in a study by Fleshman *et al.*[11] the predominance of the right lung, especially the right upper lobe was demonstrated, which differed from the general experience.

The incidence of bronchiectasis has decreased due to vaccination and effective treatment of infections in developed countries. However, it is still an important cause of chronic suppurative pulmonary disease in developing countries.[10] The most common cause of bronchiectasis among the identified cases in our report was infection, including tuberculosis. A different study from Turkey also showed that infection was the most common cause of bronchiectasis in children, with a percentage of 34.8 in the south-east of the country.[10] This shows that

infection is still the most important reason for development of bronchiectasis in our country. Among other reports, Fleshman *et al.*[11] reviewed the clinical histories of 100 Alaska native children with bronchiectasis in 1968 and found that half were non-tuberculous. Among those 49 patients, 35 had pneumonia, five had measles, three had pertussis, one had *Echinococcus granulosus*, and 18 had undetermined causes. In a study by Singleton *et al.*[12] recurrent pneumonia was obtained in 86 per cent of patients as a preceding medical event in Alaska native children; 80 per cent of those had at least one documented pneumonia or other lower respiratory tract infection in the first year of life before the diagnosis of bronchiectasis was made, and a majority of pneumonias did not have a pathogen. In our series, there were no cases with histories of known pertussis or measles. However, the presence of tuberculosis as a cause of bronchiectasis in our series was noticeable. Tuberculosis has not been considered as a cause of bronchiectasis in recent decades, because of a decrease in primary pulmonary tuberculosis and improved treatment regimens.[10] But as seen from our report, it can still be an important cause of bronchiectasis in children and can be a threatening condition for the development of bronchiectasis unless its spread is controlled and appropriate treatment is established.

There are numerous causes of bronchiectasis; however, despite extensive investigations, the underlying disease for this disorder remains unidentified in some cases. A disorder such as congenital malformations, ciliary defects or immunodeficiency could be identified in 63 per cent of children in one study.[13] A study from New Zealand showed that the cause of bronchiectasis could not be found in 50 per cent of children.[14] In another report from north-west Turkey, only 40 per cent of patients with bronchiectasis had an underlying cause and immunodeficiency, measles, ciliary dyskinesia, asthma, foreign body aspiration, and chronic aspiration syndromes were the main identified causes.[15] In this report, we were able to determine the etiology of bronchiectasis in only 51 per cent of our patients. The high prevalence of consanguinity in our patients may suggest a genetic cause for 'idiopathic' bronchiectasis, which needs further study.

In conclusion, it was found in this study that among the identified causes, the most common disease that caused bronchiectasis was infection. Besides non-specific infection, tuberculosis was an important cause of bronchiectasis. It is possible to prevent bronchiectasis in children with vaccinations and improved nutrition in developing countries. In addition, early diagnosis and treatment will increase the quality of life and survival of patients with bronchiectasis, which has irreversible and progressive complications if untreated.

References

1. Dağlı E. Non cystic bronchiectasis. Pediatr Respir Rev 2000; 1: 64–70.
2. Barker AF, Bardana EJ. Bronchiectasis: update of an orphan disease. Am Rev Respir Dis 1988; 137: 959–78.
3. Clark N. Bronchiectasis in childhood. Br Med J 1963; 1: 80–87.
4. Lewiston NJ. Bronchiectasis. In: Hilman BC (ed.), Pediatric Respiratory Disease. WB Saunders, Philadelphia, 1993; 222–29.
5. Callahan CW, Gregory JR. Bronchiectasis in children: orphan disease or persistent problem? Pediatr Pulmonol 2002; 33: 492–96.
6. Field CE. Bronchiectasis: third report on a follow-up study of medical and surgical cases from childhood. Arch Dis Child 1969; 44: 551–61.
7. Annest LS, Kratz JM, Crawford FA. Current results of treatment of bronchiectasis. J Thorac Cardiovasc Surg 1982; 83: 546–50.
8. Franklin AW. The prognosis of bronchiectasis in childhood. Arch Dis Child 1958; 33: 19–23.
9. Lewiston NM. Bronchiectasis in childhood. Pediatr Clin North Am 1984; 31: 865–78.
10. Karakoç GB, Yılmaz M, Altıntaş DU, Kendirli SG. Bronchiectasis: still a problem. Pediatr Pulmonol 2001; 32: 175–78.
11. Fleshman KJ, Wilson JF, Cohen JJ. Bronchiectasis in Alaska native children. Arch Environ Health 1968; 17: 517–23.
12. Singleton R, Morris A, Redding G, *et al*. Bronchiectasis in Alaska Native children: causes and clinical courses, Pediatr Pulmonol 2000; 29: 182–7.
13. Nikolaizik WH, Warner JO. Atetiology of chronic suppurative lung disease. Arch Dis Child 1994; 70: 141–42.
14. Edwards EA, Asher MI, Byrnes CA. Pediatric bronchiectasis in the twenty-first century: experience of a tertiary children's hospital in New Zealand. J Pediatr Child Health 2003; 39: 111–17.
15. Karakoç F, Dağlı E, Günay I, *et al*. The outcome and long term follow-up of children with bronchiectasis. Eur Respir J 1997; 10: 338s.