Clinical Analysis of Bronchiectasis in Taiwanese Children

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Background: The clinical features and etiology of bronchiectasis have rarely been described in non-Caucasian populations, of whom the prevalence of cystic fibrosis is low. In this report, we studied the clinical features of bronchiectasis in Taiwanese children.

Methods: Using a retrospective chart review, 29 cases of bronchiectasis were diagnosed from 1991 through 2001. For each case, the diagnosis was confirmed using high-resolution computed tomography. Medical records were analyzed for demographic data, clinical presentation, spirometric data, and microbial isolation. Radiographic findings were reviewed, and possible causes of bronchiectasis were also identified.

Results: There were 17 girls and 12 boys enrolled. Persistent cough, daily sputum production, and hemoptysis were common presenting symptoms. Crackles and wheezing were the most frequent findings during the physical examination. Previous lower airway infection, asthma, and primary immunodeficiency were the most common, but 31.0% of the cases had unknown causes. Dependent lobes were involved more frequently. Simultaneous sinusitis was noted in 70.6% of the cases. Spirometry showed mild airway obstruction in most of the cases. Most specimens (52.2%) from lower airway secretions yielded bacterial pathogens, most commonly *Pseudomonas aeruginosa, Haemophilus influenzae* and *Streptococcus pneumoniae*.

Conclusion: Continuing post-infectious inflammatory changes remains the most important cause of bronchiectasis in a non-Caucasian pediatric population in Northern Taiwan in the 1990s. More than two thirds of these patients had underlying predisposing factors including asthma, immunodeficiency, and swallowing dysfunction. Chronic productive purulent respiratory secretions and persistent crackles should raise the possibility of bronchiectasis in children even in Taiwan where the incidence of cystic fibrosis is low.
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Key words: **bronchiectasis, children.**

Bronchiectasis is a chronic progressive lung condition characterized by irreversible dilation of diseased bronchus.(1) In developing countries, bronchiecatsis was thought to have declined with the advent of early antibiotic usage against lower airway infections and widespread immunization against measles and pertussis. However, it is still a problem in developing countries and specific ethnic groups, such as Alaskan natives.(2) The pathogenesis and therapy of bronchiectasis has often been neglected

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and has even been called the "orphan disease".[1]

In Western countries after the World War II, more than two thirds of all cases of bronchiectasis were caused by cystic fibrosis.[3,4] To the best of our knowledge no comprehensive review of the clinical features of bronchiectasis has been published about a non-Caucasian population of Taiwanese children. We retrospectively reviewed 29 cases of bronchiectasis from 1991 through 2001 in a tertiary children's hospital in northern Taiwan and integrated the clinical, etiological, radiographic, and spirometric features in this non-Caucasian pediatric population.

METHODS

A retrospective review of patients, aged less than 18 years of age, with a diagnosis of bronchiectasis from 1991 through 2001 at Chang Gung Children's Hospital (CGCH) was carried out. The CGCH serves a dual function as a primary hospital for the local area and a referral center for the surrounding areas with a population of approximately 2 million and admits 20000 children per year. All of the children with the diagnosis of bronchiectasis were selected for analysis after a search of the medical records.

Bronchiectasis was confirmed using results of the high-resolution computed tomography (HRCT) scans. The diagnosis of bronchiectasis was based on bronchial dilatation with abnormal bronchial tapering, bronchial wall thickening, or mucus plugging in small peripheral airways observed in HRCT.[5-9]

The medical records were reviewed for demographic data, clinical presentation, spirometric data, and microbial isolation. The radiographic findings, such as HRCT and chest frontal view, were reviewed and located the areas of the lesions. Immunological survey and electromicroscopic findings were also analyzed when reports were available.

RESULTS

A total of 29 children with a diagnosis of bronchiectasis by chart review were enrolled in this study. Thirteen patients (44.8%) had spirometric results, 24 (82.7%) had immunological investigations, and seven (24.1%) had received sweat chloride test. Microbiologic studies, including bacterial and fungal cultures of sputum, found positive results in 23 children (79.3%). The sputum was obtained by bronchoalveolar lavage or cough induction. Nasal biopsy for electromicroscopic examination was performed in three children (10.3%).

Demographic data

There were 17 girls and 12 boys. The mean age of all the patients was 11.0±3.9 years. Figure 1 shows the age distribution of such patients. The majority of the patients were 5 to 12 years old (65.5%). No patient was younger than 4 years of age.

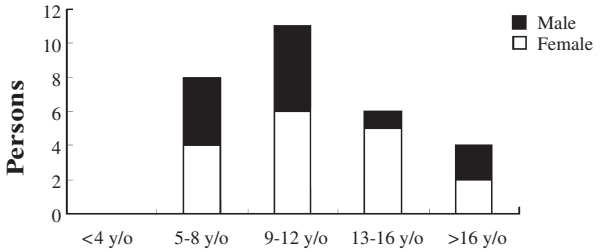

Fig. 1 Age distribution of the 29 children with bronchiectasis in CGCH.

Symptoms and signs

As shown in Table 1, chronic cough was the most common presenting symptom and affected 93.1% of the patients. Of the 26 patients who had chronic cough, 16 (59.2%) produced daily sputum. Hemoptysis was found in 12 children (41.4%). Dyspnea was seen in three patients (10.3%).

Inspiratory crackles were noted in 75.9 % of patients. Wheezing and rhonchi were found in 10 (34.5%) and eight (27.6%), respectively. Digital clubbing was found in 20.7% of cases. Normal physical examination results were noted in two patients (6.8%).

Etiology and predisposing illness

Antecedent lung injury was caused by previous lower airway infections, bronchopneumonia or pneumonia in eight infants or toddlers (Table 2). *Bordetella pertussis* (N=2) and *Mycobacterium tuberculosis* (N=2) were the causes of precipitating airway inflammation and destruction. No preceding infectious pathogens attributing to the long-term continuing inflammation were found in the other four

Table 1. Symptoms and Signs of Bronchiectasis in 29 Children

	No. (%)
Symptoms	
Cough	26/29 (93.1%)
Daily sputum	16/29 (55.2%)
Dyspnea	3/29 (10.3%)
Hemoptysis	12/29 (41.4%)
Signs	
Crackles	22/29 (75.9%)
Wheezes	10/29 (34.5%)
Rhonchi	8/29 (27.6%)
Clubbing fingers	6/29 (20.7%)
Normal findings	2/29 (6.8%)

Table 2. Underlying Illness of Bronchiectasis

Etiology	No. (%)
Previous lower airway infection*	8/29 (27.6%)
Asthma	4/29 (13.8%)
Immunodeficiency†	3/29 (10.3%)
Aspiration syndrome	2/29 (6.9%)
Ciliary dyskinesia	1/29 (3.4%)
Cystic fibrosis	1/29 (3.4%)
Marfan's syndrome	1/29 (3.4%)
Unknown causes	9/29 (31.0%)

*: Two following pertussis and two following pulmonary tuberculosis.

†: One with IgG3 deficiency and two with common variable immunodeficiency

patients. Four children (13.8%) had recalcitrant asthma but bronchiectasis subsequently developed 2 to 4 years after diagnosis. Specific IgE for Aspergillus was negative in these four patients. Three (10.3%) had immunological abnormalities; one had immunoglobulin G_3 deficiency and two had common variable immunodeficiency. Chronic aspirations causing bronchiectasis were suggested in two children with cerebral palsy. One patient had primary ciliary dyskinesia as confirmed by nasal mucosal biopsy. Cystic fibrosis was suggested in a 9-year-old boy who presented with bronchiectasis, sinusitis, and rectal prolapse using an elevation of sweat chloride test (> 80 mEq/L). One patient had spontaneous pneumothorax and developed bronchiectasis 1 year afterward. No antecedent lung injury was suggested in nine patients (31.0%) even after thorough investigation for the cause of bronchiectasis.

Spirometry

Spirometry was performed in 13 patients. Forced vital capacity (FVC) was universally normal (82.5±39.1%). Reduced forced expiratory volume in one second (FEV1) and FEV1/FVC were found in these patients (67.6±43.8% and 67.5±27.7% respectively).

Table 3. Localization of Bronchiectasis and Co-Morbid Sinusitis

No. (%)	
Location of lesions	
Left lower lobe	26/29 (89.7%)
Right lower lobe	20/29 (69.0%)
Right middle lobe	13/29 (44.8%)
Right upper lobe	10/29 (34.5%)
Left upper lobe	5/29 (17.2%)
Sinusitis	12/17 (70.6%)

Table 4. Findings in Chest Radiograph of 29 Children with Bronchiectasis

Radiographic Signs	No. (%)
Loss of definition of vessel markings	27/29 (93.1%)
Collapse or atelectasis	16/29 (55.2%)
Ring shadows	8/29 (27.6%)
Hyperinflation	4/29 (13.8%)
Normal findings	2/29 (6.9%)

Radiographic findings

Left lower lobe and right lower lobe involvement were seen in 89.7% and 69.0% of patients, respectively. Single lobar involvement was found in three patients (10.3%; Table 3).

Chest radiographs (CxR) were reviewed by a competent pediatric radiologist. As shown in Table 4, loss of definition of vessel marking was found in 27 patients (93.1%). Lobar collapse or segmental atelectasis was found in 55.2% of patients. Ring-shadow with or without air-fluid level occurred in 27.6% of patients. Only 6.9% of these patients showed normal CxR.

Water's view for maxillary sinus was performed in 17 of the patients. Opacity or cloudiness was found in 11 patients (70.6%) who received sinus radiography.

Microbiologic reports

Cultures of sputum or bronchoalveolar lavage fluid were available for 23 of these patients. Pathogens were found in the 12 of the 23 patients (52.2%). Two patients had polymicrobial (one with

Candida albicans and Aspergillus, another with *Candida albicans* and *Pseudomonas aeruginosa*), and 10 had single pathogen isolated. *Pseudomonas aeruginosa* was cultured in three patients. *Haemophilus influenzae* and *Streptococcus pneumoniae* were found in two patients each. Infection by *Mycoplasma pneumoniae* was suggested in three patients according to the serologic results of positive findings of IgM.

DISCUSSION

The majority of the children suffering from bronchiectasis were in the 5- to 12-year-old age group in this study. The decreased number of patients older than 16 years of age may be explained by a selection bias because adolescent patients tend to visit adult respiratory clinics instead of visiting pediatric department. For patients below 4 years of age, few pediatricians considered bronchiectasis in such instances and HRCT was not regularly performed. Interestingly, a female predominance that has not been mentioned previously, except in a study in aging adults, was noted in our patients.[10] The cause of this observation remains elusive.

Our review of the symptoms and signs in this group of patients indicates the presence of chronic cough with daily sputum production and audible crackles upon auscultation of involved lobes were the first clues of bronchiectasis. The occurrence of hemoptysis in 41.4% of our patients was more frequent when compared with other reports on pediatric patients but more comparable with the adult population.[10-12] This difference was thought to be because there were no quantitative descriptions for the severity of hemoptysis in these studies. Clubbing of digits (20.7%) was less frequent than that reported in earlier studies (44% in the study by Field and 33.6% in the study by Clark).[11,12] It may be explained by the low prevalence of cystic fibrosis in Taiwan, early and easy access of medical facilities in our area. Two patients with typical symptoms had normal physical findings. This emphasizes the importance of typical clinical symptoms in the diagnosis of bronchiectasis.

Underlying diseases were found in more than two thirds of our patients. In 1994, Nikolaizik and Warner reported 41 children with chronic suppurative lung diseases, when excluding cases of cystic fibrosis, they revealed that six patients (15%) had underlying congenital malformations, seven (17%) had primary ciliary dyskinesia syndrome, 11 (27%) had immune deficiency, two (5%) had foreign body aspiration, and 15 (36%) had no underlying diseases.[13] Similarly, preceding infections of lower airway was a major factor in our study. Although the rate of routine immunization for measles and pertussis in Taiwan was more than 90%, bronchiectasis following pertussis was found in two children with positive vaccination history. Inadequate protective efficacy due to failure of serum conversion after vaccination or decline in antibody titer should be considered. Tuberculosis has been an important cause of post-infectious bronchiectasis worldwide.[1,14] Pulmonary tuberculosis is still prevalent in northern Taiwan and two children had pulmonary tuberculosis in this series.[15]

Cystic fibrosis is the most common cause of bronchiectasis in the Caucasian population.[2] According to a study based on a Hawaiian population, the prevalence of cystic fibrosis is thought to be less than 1 in 90000 live births among Asians.[16] It was thought to be even more rare in the Chinese population.[17,18] The only suggested patient in this study revealed an elevated sweat chloride, but no further genetic study was done. The mutations of the Asian population are different from that of the Caucasian population at ΔF508.[19]

Immunodeficiency played an important role in the development of bronchiectasis in the 1990s. Compared with the report of Nikolaizik,[4] fewer patients with immunodeficiency were noted in our study. This difference may be associated with the incompletely immune study and inadequate patient numbers in this study. Gracia et al reported 31 patients with bronchiectastic with IgG subclass deficiency; IgG_2 deficiency was the most common among them.[20] However in the only one case with IgG subclass deficiency among our patients, the definite subclass deficit was IgG_3.

The association of asthma and bronchiectasis has been questioned for years. The prevalence of asthma in patients with bronchiectasis varied between 2.7% and 27% in reports from Hong Kong.[21,22] It has been postulated that either inadequacy of asthma therapy or persistent airflow narrowing from recurrent exacerbations was the precipitating cause of bronchiectasis. In a report from Finland,[23] asthma was also prevalent (19%) in hospi-

talized patients with bronchiectasis. Allergic bronchopulmonary aspergillosis is a well-known cause in patients with asthma and bronchiectasis. None of our four patients with asthma showed evidence of allergic bronchopulmonary aspergillosis. The association of bronchiectasis remains unknown at the present time.

Aspiration of gastric contents or colonized flora of the pharyngeal cavity was thought to initiate inflammation and result in acute and long-term airway damage.[1] Two patients had cerebral palsy in this study. The comorbid swallowing dysfunction was considered to be a possible etiology of bronchiectasis.

Spontaneous pneumothorax and bronchiecatsis in patients with Marfan syndrome has been reported.[24,25] Connective tissue weakness and increased susceptibility to pulmonary infections were thought to be contributing factors to bronchiectasis.[25]

Nowadays CxR is seldom used as a diagnostic tool of bronchiectasis because most cases are detected early with mild bronchiectasis. In the study of Kornreich et al.,[26] none of the 25 children with positive CT for bronchiectasis had normal CxR. In our study, the common CxR signs were loss of definition of vessel marking and atelectasis. Normal CxR results were found in only 6.9% of the 29 patients. These results are different with those experienced in adults,[27] which indicated only a minority of patients with CxR abnormalities.

Mild limitations of airflow with a reduced FEV1/FVC, normal FVC, and reduced FEV1, were found in our patients. Compared with results of previous reports in adult and adolescent patients,[3,11] we believe that mild airway obstruction observed in this study might be due to shorter duration of illness and milder degree of airway destruction as compared with a population with high incidence of cystic fibrosis.

A wide variety of organisms were found in our study. Our results were consistent with those of earlier reports from adults which found *Pseudomonas aeruginosa, Hemophilus influenzae* and *Streptococcus pneumoniae* were the most commonly isolated microorganisms.[11,28] Other low-grade pathogens such as the fungi and atypical mycobacteria were also reported in elderly patients with bronchiectasis.[10] Aspergillus and *Candida albican* were also found in our study.

In this study, we depicted the clinical features of children with bronchiectasis in northern Taiwan where the prevalence of cystic fibrosis is very low. Post-infectious insult is the most important factor of bronchiectasis in a non-Caucasian pediatric population, following pertussis and infections despite the high vaccination rate for pertussis and bacillus Calmette-Guerin. More than two thirds of our patients had underlying causes in children with bronchiectasis and required thorough investigations including asthma, immunoglobulin deficiency, swallowing disturbance and cilia dyskinesia syndrome. Chronic cough with daily sputum production and persistent audible crackles remain the most valuable clues to early diagnosis of bronchiectasis.

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台灣兒童支氣管擴張症之臨床分析

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背 景： 在囊狀纖維化 (cystic fibrosis) 盛行率極低之非高加索人兒童中，支氣管擴張症之臨床表現及致病原因在過去罕爲描述。此份報告旨在描述台灣兒童支氣管擴張症之臨床特徵。

方 法： 經由回溯性的病歷分析，自1991年到2001年中計有29例診斷爲支氣管擴張症之兒童。每一例皆由高解析度電腦斷層獲得診斷。藉由病歷記錄分析其基本資料，臨床表現，肺功能報告與微生物檢查。我們亦檢視其放射學檢查，並儘可能探究造成支氣管擴張症之原因。

結 果： 此次研究中計有17個女孩及12個男孩，平均年齡11.0±3.9歲。持續性之慢性咳嗽，終日之痰液生成與咳血爲常見症狀。肺囉音與喘鳴音爲理學檢查中最常見之發現。先前之下呼吸道感染，氣喘與原發性之免疫功能缺損爲常見之致病因，但仍有31.0%的病例查不出可能致病因。居下位的肺葉爲常影響之位置，有89.7%的病童左下葉，右下葉亦有69.0%；而同時合併有鼻竇炎者亦佔70.6%。在接受肺功能檢查之病童中，大部分皆呈現輕度之呼吸道阻塞。從痰液或支氣管肺泡沖洗液之微生物檢查中，大部分檢體 (52.2%) 有發現；其中*Pseudomonas aeruginosa, Hemophilus influenzae*和*Streptococcus pneumoniae*爲常見病菌。

結 論: 就90年代非高加索族群的北台灣兒童而言，下呼吸道感染後的持續性發炎變化仍是支氣管擴張症的重要原因。超過三分之二的病童有其潛在之易致病因子，諸如氣喘，免疫功能缺損及吞嚥障礙。即使在此囊狀纖維化盛行率極低之地區，凡兒童有慢性化膿性之痰液生成和持續的肺囉音時，皆必須考慮支氣管擴張症的可能。

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關鍵字: 支氣管擴張症，兒童。

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