

Original Article

Non-cystic Fibrosis Bronchiectasis: the Experience in Saudi Arabia

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ABSTRACT

Objective: To review the etiological factors and associated diseases of Non-cystic fibrosis bronchiectasis (NCFB)

Design: A retrospective cohort study of all patients with confirmed NCFB by chest X-ray and/or CT chest in a pulmonary clinic for the period 1993-2005.

Setting: A tertiary care center in Riyadh, Saudi Arabia.

Subjects: Children less than 14 years of age with NCFB
Main Outcome Measures: Association with other diseases, radiological pattern, bacteriological pattern and pulmonary function test abnormalities (PFT).

Results: A total of 151 cases were diagnosed with NCFB. 75 (49.7%) were male, 76(50.3%) were female. 148(98%) are alive. More than 2/3 of the patients had cough,

tachypnea, wheezing, sputum production and failure to thrive. 91 (60%) had associated diseases: pulmonary diseases in 48 (32%), immunodeficiency in 27 (18%), CNS in 10 (7%), cardiac in 10 (7%), and asthma in 103 (68%) of the patients. Left lower lobes was commonly involved in 114 (76%). 68 (67%) were found to have sinusitis. Fourty-nine (32%) developed gastroesophageal reflux (GER). *Hemophilus influenza* was cultured in 56 (37%), *Strept pneumoniae* in 25 (17%), and *Pseudomonas aeruginosa* in 24 (16%) of the patients. 80% of the patients who had PFT had abnormal changes.

Conclusion: NCFB is a common problem in Saudi Arabia. Early diagnosis and identification of associated diseases is needed to prevent progression of the disease.

KEY WORDS: bronchiectasis, chest infection, developing countries

INTRODUCTION

Bronchiectasis was called an orphan disease for the last two decades as its incidence decreased markedly and it became an uncommon clinical entity among adults and children in developed countries^[1]. It is defined as a permanent dilatation of the bronchi that typically involves the second to sixth order of segmental bronchi^[2]. It was first described by Laennec in 1819 based on examination of postmortem specimens^[3]. Bierring (1956) studied 151 patients in Copenhagen following pneumonia and found only one child (0.7 %) to have bronchiectasis^[4]. Ruberman and colleagues (1957) evaluated 69 patients with persistent abnormalities on chest radiographs by bronchoscopy^[5]. Out of 1711 young adults (18 to 25 years of age) treated for pneumonia at a U.S. army hospital, 29 (1.7%) were found to have bronchiectatic changes^[5]. Field noted a dramatic decrease in admission rates for bronchiectasis at five British hospitals from an average of 48 per 10,000 in 1952 to 10 per 10,000 pediatric admissions in 1960^[6]. She speculated that this was due to improved treatment

of lower respiratory tract infections made possible by the increased availability of broad-spectrum antibiotics during that period^[6]. Other contributing factors include the prevention of measles and pertussis through immunization and the marked decrease in primary pulmonary tuberculosis in the pediatric population brought about by better public health measures and improved treatment regimens for this disease^[3]. The incidence of childhood bronchiectasis has been documented to have an ongoing decline in the literature^[2]. Clark summarized many series from 1900 - 1950s and in his own report of 116 children in 1963^[7] noted that half of the children developed bronchiectasis following severe pneumonia. He estimated the annual incidence of bronchiectasis to be 1.06/10,000 children. Most series indicate a male/ female ratio about 1:1.4^[1-6].

In this report, we present the experience of a tertiary care center in Saudi Arabia on childhood bronchiectasis and review the etiological factors and associated diseases of Non-cystic fibrosis bronchiectasis (NCFB).

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SUBJECTS AND METHODS

We undertook a retrospective review of the medical records for all patients referred to the pulmonary clinic for evaluation of recurrent chest infection from January 1993 to August 2005 at the King Faisal specialist hospital and research center (KFSH & RC) in Riyadh region. This center is considered a tertiary care center for referral of complicated cases in Saudi Arabia. Demographic, radiological patterns, associated diseases, and pulmonary function test (PFT) data were collected.

Patient management: All confirmed cases of bronchiectasis were screened for cystic fibrosis by sweat chloride test, PPD skin test, respiratory cultures for virology, acid-fast bacilli and other pathogenic bacteria. They were followed-up every 1-3 month according to the severity of their disease. They were taught how to do regular chest physiotherapy to mobilize secretion and how to self-administer salbutamol and inhaled steroid according to their need. Antibiotic treatment orally or intravenously was advised during exacerbation of their symptoms (increasing cough, sputum production, change in the color of their sputum to yellowish or greenish or respiratory distress).

Patients who showed clinical deterioration in the form of recurrent fever, increase in sputum or cough, and radiological deterioration in the form of involvement of another lobe with bronchiectatic changes or PFT deterioration in all parameters, were admitted to the hospital for intensive chest intravenous physiotherapy, airway clearance and antibiotics (according to bacterial organism from the respiratory cultures) for approximately 7-10 days, in addition to inhaled albuterol and steroid.

Lobectomy was done to prevent deterioration when medical treatment failed to stabilize PFT and radiological pictures. It was usually done in the most severely affected lobe radiologically.

Statistical analysis: SPSS program for Windows (release 11.0.0) was used for data analysis. Chi-Square (X^2) was used to compare categorical variables. The level for statistical significance was a p-value 0.05.

DEFINITIONS

Progression of disease: is a qualitative measurement, defined as a radiological deterioration with more lobes involved in addition to clinical deterioration with increased sputum production, cough and / or fever.

PFT severity is a quantitative measurement of airflow in PFT:

Mild lung changes: defined as forced expiratory volume in one second (FEV1) = 65 - 75% of predicted values

Moderate lung changes: FEV1 = 55 - 65% predicted

Severe lung changes: FEV1 < 55% predicted

RESULTS

Out of a total of 900 cases referred with recurrent chest infection to the pulmonary clinic from January 1993 to August 2005, 200 patients were diagnosed to have cystic fibrosis (CF). Of the remaining 700, 151 cases were diagnosed as NCF bronchiectasis (based on high resolution CT of the chest in 145 cases, 96% and chest X-ray in six cases, 4%) due to severe bilateral cystic dilatation of bronchi. Seventy-five (49.7%) were male and 76 (50.3%) were female. One hundred and forty eight (98%) are alive and three (2%) have died. One hundred and forty-four (95%) were Saudi nationals and seven (5%) non - Saudi. One-hundred and forty (93%) were full term. Twenty-two (14.6%) were from the eastern region, 26 (17.2%) from the central region, 39 (25.8%) from the western region, 33 (21.9%) from the southern region and four (2.6%) from neighboring countries. Ninety-eight (65%) patients had consanguineous parents. Eighteen patients (12%) had one or two siblings with bronchiectasis and five patients had three to four siblings with similar disease. The age at which symptoms started was 2.3 ± 2.2 years. The age for referral to our center was 6.3 ± 4 years. The age at which bronchiectasis was diagnosed was 7.3 ± 4.1 years. There was usually a period of 5 ± 3.2 years between the start of symptoms to the diagnosis of bronchiectasis. The period of follow up was 5.5 ± 3.9 years.

Clinical presentations: More than two thirds of patients presented with cough, tachypnea, wheezing, sputum production and failure to thrive. Clubbing was found in 50 (33%) patients. Cyanosis and oxygen requirement was reported in 35 (23%) patients. Hemoptysis was only reported in seven (5%) cases.

Underlying etiology: Ninety-one (60%) had associated diseases (Table 1). Pulmonary diseases were found in 48 (32%), immunodeficiency in 27 (18%) (Fig. 1), central nervous system (CNS) involvement in 10 (7%), cardiac involvement in 10 (7%), skeletal anomalies in 10 (7%) and asthma in 103 (68%) patients (Table 1). More than two-third patients had two or more associated diseases.

Radiological findings: The following were reported: consolidation of one or two lobes in 137 (91%), compensatory hyperinflation in 103 (68%), interstitial

Table 1: Bronchiectasis and disease association (n = 91, 60%)

Disease association	n (%)	Disease association	n (%)
Pulmonary:		Immunodeficiency:	
Kartagener	4 (4)	Hypogammaglobulinemia	3 (3)
FBA	6 (7)	SCIDS	3 (3)
Immotile cilia syndrome	17 (19)	HIV	1 (1)
Lipid pneumonia	7 (8)	Hyper IgE	1 (1)
Interstitial pneumonia	2 (2)	IgG subclass deficiency	6 (7)
ABPA	2 (2)	Hyper IgM	2 (2)
T.B.	2 (2)	Whiscott Aldrich syndrome	1 (1)
RMLsyndrome	1 (1)	Poor antibodies response	4 (4)
TEF repair	4 (4)	Common variable-	
Bronchogenic cyst	2 (2)	hypogammaglobulinemia	3 (3)
Cystic lung disease	5 (5)	T-cell deficiency	3 (3)
Lung collapse	3 (3)	Barre lymphocyte syndrome	1 (1)
Prematurity	3 (3)		
Cardiac Diseases:		Central nervous system disease:	
Dextrocardia	4 (4)	Cerebral palsy/seizure disorder	4 (4)
Congestive heart failure	1 (1)	Apnea	1 (1)
Ventricular septal defect	2 (2)	Craniosynostosis	1 (1)
Atrial septal defect	1 (1)	Cutis laxa/developmental delay	1 (1)
Pulmonary hypertension	1 (1)	Down syndrome/ Seizure	2 (2)
Mitral valve prolapse	1 (1)	Fatty acid oxidation defect	1 (1)
Skeletal:		Other disease associations:	
Pectus excavatum	2 (2)	Neuroblastoma	1 (1)
Scoliosis	4 (4)	Antithrombin III deficiency	2 (2)
Absent ribs	3 (2)	Corrosive ingestion	2 (2)
Marfan's syndrome	1 (1)	Liver cirrhosis	1 (1)
		Ethmoid mucocele	1 (1)
		Bullous skin lesion/septicemia	1 (1)

FBA= Foreign body aspiration

ABPA= Allergic bronchopulmonary aspergillosis

TB = Tuberculosis

RML= Right middle lobe

TEF = Tracheoesophageal fistula

SCIDS = Severe combined immunodeficiency

pattern in 49 (33%), atelectasis in 117 (78%), peribronchial wall thickening in 115 (76%) and lymph node enlargement of the paratracheal region in 33 (22%) patients. Left lower lobes (LLL) was involved in 114 (76%), right middle lobe (RML) in 82 (54%), and right lower lobe (RLL) in 76 (50%), lingula in 73 (48%), right upper lobe (RUL) in 39 (26%), and left upper lobe (LUL) in 27 (18%) patients. More than two-third patients had more than two lobes affected with bronchiectasis. Bilateral lobar involvement was seen in 112 (71%) patients.

Bronchoscopy was done in 20 out of 117 patients who had persistent atelectasis of the affected lobes and showed no evidence of foreign body aspiration. The remaining 97 patients had partial improvement of the atelectatic lobes. A total of 102 patients had sinus X-ray and 18 (12%) had CT scan of the sinuses. Sixty-eight (67%) out of 102 patients "who had sinus radiological investigations" were found to have sinusitis. Gastroesophageal reflux (GER) was diagnosed in 49 (32%) patients: thirty -

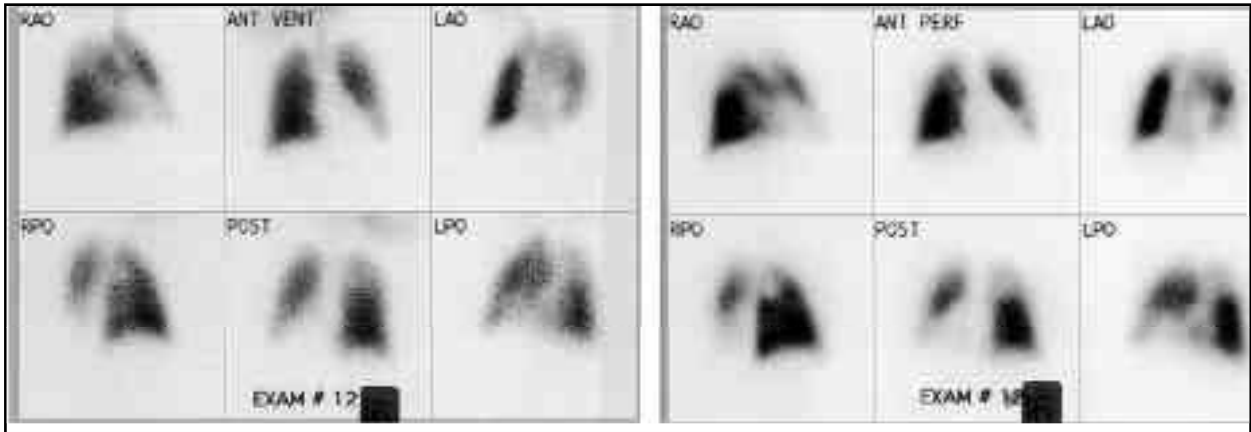
Fig. 1: A patient with common variable hypogammaglobulinemia, and LLLbronchiectasis

1A: CT chest showing mild dilatation in the posterior aspect of the LLL with failure of normal tapering when the bronchi are approaching the periphery of the lung. The bronchi also show some crowding.

three patients by barium swallow alone, 10 patients by milk scan alone and six patients by both radiological procedures. Twenty-two of the 49 patients with GER (45%) required Nissen fundoplication.

Types of organisms: Respiratory cultures were done in 105 (70%) patients by sputum cultures (if patients were able to produce sputum) or by nasopharyngeal aspirates (for patients less than four years). The following were grown: *Mycobacterium tuberculosis* in one patient, *Hemophilus influenza* (H-flue) was cultured in 56 (37%), *Streptococcus pneumoniae* in 25 (17%), *Pseudomonas aeruginosa* in 24 (16%), *Branhamella cattarrhales* in 13 (9%), *Staphylococcus aureus* (Staph.) in 11 (7%) and Methicillin resistant *Staphylococcus aureus* (MRSA) in three (2%) patients. *Candida albicans* was grown in two (1%) patients. About 50% patients had more than one organism simultaneously. Viral cultures were done in 33 (22%) patients: respiratory syncytial virus in was found in three (9%), and enterovirus in one (3%) patient.

PFT: Seventy-seven (49%) patients were able to do pulmonary function test (PFT). Sixty-eight (88%) of them had abnormal PFT results. Seventeen (22%) had obstructive lung changes, 14 (18%) had restrictive lung changes and 37 (48%) had combined obstructive and restrictive lung changes. Mean values \pm SD (standard deviation) were as follows: FVC (forced vital capacity) = 67 ± 19 , FEV1 (forced expiratory volume in one second) = 65 ± 2 , FEV1 / FVC ratio = 98 ± 16 , MMEF = $25 - 75\%$ (maximum mid expiratory flow) = 53 ± 27 , peak expiratory flow = 67 ± 20 , FRC (functional residual capacity) = 106 ± 21 , RV (residual volume) = 152 ± 40 , RV / TLC ratio = 46 ± 1 and RV / TLC% = $180 \pm$



1B: V/Q lungs scan: There is large defect in the LLL, which is matched in ventilation and perfusion. The ventilation defect is slightly worse than the perfusion defect.

45. Sixteen (21%) had mild air flow limitation, 30 (39%) moderate air flow limitation and 22 (28.5%) had severe air flow limitation.

Prognosis: Disease progression developed in 72 (48%) patients and it was related to the development of symptoms before five years of age, persistent atelectasis of the affected lobes and involvement of RLL with bronchiectasis ($p < 0.05$). Unilateral lobectomy was done in 21 (14%) patients whereas bilateral lobectomies were performed in three (2%) patients. Follow up of patients who had lobectomy showed that in 16 out of 21 patients, clinical, radiological and PFT status had improved, while in five patients it had deteriorated due to other associated diseases. Recurrent otitis media was reported in 12 (8%) patients. All three patients who died developed acute lung infection in a local hospital that required ventilation and progressed to respiratory failure and death. One of them who died at 16 years of age had repair of esophageal atresia and tracheo - esophageal fistula with esophageal - colonic anastomosis and recurrent aspiration that required right pneumonectomy. The second patient had hype IgM syndrome with lympho - proliferative disorder and CMV infection. The third patient had lipid pneumonia that was complicated with bilateral necrotizing pneumonia, bilateral pneumothoraces, chronic ventilation that required tracheostomy, acute hepatitis, staphylococcal septicemia, and recurrent pleural effusion and died at four years of age.

DISCUSSION

A recent review of bronchiectasis among Alaska native children residing in the Yukon-Kuskowkim delta region reported a persistently high incidence of 110 / 10,000 in 1940s and 140 / 10,000 persons born in the 1980s^[8]. Alaska is considered part of a developed nation, with adequate immunization programs, and tuberculosis is no longer a major

source of pulmonary disease. However, the children reported lived in conditions of relative poverty: small crowded houses heated by wood-burning stoves, with limited access to running water, and 70% of households had one or more family members who smoked tobacco which promotes chronic airway mucous secretion and recurrent respiratory infections^[10,11].

Published reports from some developing countries suggest that childhood bronchiectasis may not be disappearing, and that it represents a more common problem than in developed countries^[12]. Karakoc from Turkey described 23 children with bronchiectasis and found that factors other than infections have contributed to the development of bronchiectasis, such as immunodeficiency, primary ciliary dyskinesia and asthma^[2]. A report by Dawson from United Arab Emirates from Abu Dhabi region described 32 children with bronchiectasis from a population of 300,000^[9]. He found that congenital anomalies of the respiratory system, prematurity, immunodeficiency were some of the factors that contributed to the cause of the disease in addition to viral or bacteria infections^[9].

In our report, the incidence of bronchiectasis was found to be one in four cases that presented with recurrent chest infection in our center, which makes it a common problem in this part of the world. Bacterial infection with the common respiratory organisms such as *Staph aureus*, H-flue, *Pneumococcus*, and *Pseudomonas* was positive in 51% of the patients. The Southwestern region accounted for 50% of the reported cases. Environmental factors such as humidity and crowdedness during pilgrimage time may have contributed to such increase in its incidence^[12]. Recurrent aspiration pneumonia due to CNS anomalies or seizure is described for the first time in the literature and might be related to recurrent aspiration of secretions due to swallowing incoordination and / or GER. Our report is in

agreement with another report of early start of symptoms before five years of age in 83% of our population^[2] with a delay of diagnosis of bronchiectasis by an average of 5 - 10 years^[12]. Most of the patients had bilateral lobar involvement and severe PFT changes at presentation. Fifty percent of our patients had radiological and clinical progression inspite of medical treatment with antibiotic prophylaxis, which may suggest the adoption of surgical intervention in patients with progressive disease. Lobectomy was done in only 16% of our population compared to 60-70% in other reports^[2,9-15]. Asthma was a common association in 68% of the patients, which is in accordance with other reports^[16-18] and treatment with inhaled steroid and 2 agonist may need to be considered in some patients. Immunodeficiency is common in our country due to consanguinity and was found to be the second most common disease association after pulmonary disease (Table 1). Sinusitis was also a common presentation in 68% cases and such patients may need to be treated for a longer period of time (4 - 6 weeks) as suggested by other reports^[9]. Persistent atelectasis of the affected lobe has been contributing to the development of bronchiectasis in our population, which may warrant encouragement of chest physiotherapy, and postural drainage in patients with such a problem. Atelectasis is commonly found in many patients with pneumonia, aspiration or asthma and repeat chest X-ray should be done after clinical improvement to ensure the re-expansion of the atelectatic part of the lung. Gastroesophageal reflux and recurrent aspiration was found in 32% of our patients and may have contributed to the development of bronchiectasis or complicated its progression^[19]. Lobectomy was done in only 16% of our patients compared to 60-70% in other reports. This is considered a small proportion in view of the excellent improvement of clinical picture seen in three-fourths of our patients who had lobectomy (16 out of 21), and may need to be considered early if medical treatment failed to improve clinical or radiological pictures^[14,15]. A case control study needs to be done to identify the actual risk factors of developing such disease in our country. Efforts should be made to diagnose it early, be aware of contributing factors, provide early treatment and referral before development of progression.

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