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Original Article

Outcome of Cystic Fibrosis in Patients with Bronchiectasis

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Abstract

Introduction
Bronchiectasis is a common problem in children especially under 5 years. Early diagnosis of disease and its causes could be useful in early treatment and preventing probable complications. This study aimed at evaluating the Cystic fibrosis (CF) in patients with bronchiectasis.

Materials and Methods
In a cross-sectional study, 374 children with bronchiectasis were studied. The diagnosis was made according to clinical (chronic cough and persistent sputum) and Computerised tomography (CT) scan findings. Demographic findings, clinical findings, treatment, etiology, imaging and outcome of diseas were recorded.

Results
Two-hundred-and-forty (64.2%) were male with mean age of 8.61±3.36 years at the diagnosis. In patients with and without the etiology of CF, the cure was observed in 1 (5.6%) and 132 (37.1%), partial remission in 5 (27.8%) and 148 (41.6%) of the cases and non improvement in 12 (66.7%) and 76 (21.3%). There was significant relation between existence of asthma ($p<0.001$), Gastroesophageal reflux (GERD) ($p=0.02$) and CF ($p<0.001$) with response to treatment in bronchiectasis.

Conclusion
Bronchiectasis is common in infants with the etiology of CF and cure and partial remission is lower in CF patients who have bronchiectasis.

Keywords: Bronchiectasis, Children, Cystic fibrosis, Outcome.

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Introduction

Bronchiectasis is a disease state defined by localized, irreversible dilation of part of the bronchial tree caused by destruction of the muscle and elastic tissue. It is classified as an obstructive lung disease, along with emphysema, bronchitis, asthma, and cystic fibrosis (1,2). Involved bronchi are dilated, inflamed, and easily collapsible, resulting in airflow obstruction and impaired clearance of secretions. Bronchiectasis is associated with a wide range of disorders, but it usually results from bacterial infections, such as infections caused by the Staphylococcus or Klebsiella species, or Bordetella pertussis (3,4). Some people with bronchiectasis may produce frequent green/yellow sputum. However, it is possible to have "dry bronchiectasis" in which there is no sputum production. Sputum production may also occur without coloration. People with bronchiectasis may have bad breath indicative of active infection. Frequent bronchial infections and breathlessness are two possible indicators of bronchiectasis (5,6). Bronchiectasis has both congenital and acquired causes, with the latter more frequent. A common genetic cause is cystic fibrosis, in which a small number of patients develop severe localized bronchiectasis (7,8). Illness and death from cystic fibrosis are due primarily to progressively destructive lung disease resulting in bronchiectasis and respiratory failure. The true prevalence of bronchiectasis among children with cystic fibrosis is unknown; however, studies conducted previously have shown that 50 to 70% of patients have CT-defined bronchiectasis by 3 to 5 years of age (9,10). Once present, bronchiectasis persists and progresses in approximately 75% of young children, despite receipt of the best current therapy. Previous studies have shown that neutrophilic inflammation are the major risk factors for early disease in cystic fibrosis, including the development and progression of bronchiectasis, a reduction in the body-mass index, and lung-function decline (11,12). BAL-based studies have shown that lung disease begins early in life and is associated with increased levels of proinflammatory cytokines, such as Interleukin 8 (IL-8) or CXCL8, and that more extensive inflammation is found in lung lobes with more severe bronchiectasis (13,14). The aim of this study was to evaluate the cystic fibrosis (CF) in patients with bronchiectasis.

Materials and Methods

This cross-sectional study was conducted on 347 children with bronchiectasis in Children Hospital, Tabriz, Iran, from May 2004 to May 2013. This study was approved by Ethic Committee of Tabriz University of Medical Sciences. Written consent was obtained from all the patients parents. The diagnosis was made according to clinical findings (chronic cough and persistent sputum) and CT scan findings. Demographic findings, clinical findings, treatment, etiology, imaging and outcome of diseas were recorded. All the patients without known causative factor who were referred to our Pulmonary Department in this period were evaluated for the diagnosis of CF by clinical assessment, sweat chloride test, analysis of the Cystic fibrosis transmembrane conductance regulator (CFTR) gene when possible. The following characteristics were assessed at time that CF was diagnosed: age, familial and personal medical history (particularly digestive problems and male infertility). Respiratory bacterial infections were evaluated using quantitative sputum cultures. Pancreatic status was determined by the fat content in stool samples collected over a 72-h period; patients with normal results (fecal fat <6 g/day) were defined as Pancreatic sufficient (PS) and

the others were defined as Pancreatic insufficient (PI). The pilocarpine iontophoresis test was performed on both arms with measurements of sweat weight. A minimum of 80 mg of sweat was analyzed. Sweat chloride concentrations were measured by the standard titrimetric method described by Gibson and Cooke. According to the guidelines for the performance of the sweat test for the investigation of CF, a sweat chloride concentration of more than 60 mmol l^{-1} supports the diagnosis of CF, intermediate chloride concentration of 40–60 mmol l^{-1} is suggestive, but not diagnostic of CF, a sweat chloride of less than 40 mmol mmol l^{-1} is normal and there is a low probability of CF. Two sweat tests were performed for each patient. Genomic DNA was extracted from whole peripheral blood samples by standard methods.

SPSS version 16 was used as statistical analysis. In our study, ANOVA was used to test whether there was a significant difference between the means of the data obtained from more than two independent groups. At the end of our study, ANOVA was performed between the data and the datasets. By means of single-factor ANOVA (Student's t-test), the changes were observed. The standard deviation coefficient has been calculated as the measure of the central dispersion, which determines the distance of the available datasets from the mean value. The purpose of the applied statistical method was to clarify the data and was called a "descriptive statistical method". By classifying the data, summary tables were created, and the mean value, standard deviation and dispersion measurements obtained. ($P<0.05$) was regarded as significant.

Results

Two-hundred-and-forty patients (64.2%) were male with mean age of 8.61 ± 3.36 years at the diagnosis. Past medical history was positive in 51 patients (13.6%) included preterm labour in 22 cases (5.9 %), recurrent pneumonia in 16 cases (4.3%), cleft lip in 4 patients (1%), collapse of a pulmonary lobe in 3 cases (0.8%), asphyxia in 3 cases (0.8%), congenital metabolic disease in 2 cases (0.5%) and pulmonary lobectomy 1 (0.3%). All 374 patients had been admitted with a cough. Cough with chronic sputum lonely was observed in 296 cases (79.1 %), with recurrent pneumonia in 14 cases (3.7 %), with dispnea in 30 cases (85), with recurrent aspiration in 1 cases (0.3 %), with tachypnea in 3 cases (0.8%), with hemoptysis in 11 patients (2.9%) of the patients.

The hemoptysis with pneumonia was observed in 8 cases (12.1%), recurrent pneumonia in 6 cases (1.6%), dyspnea in 4 (1.1%) and 1 case of pneumonia associated with collapse of the lung (0.3%). Disease etiology was asthma in 55.6%, Gastroesophageal reflux (GERD) in 7.8%, cystic fibrosis in 4.8%, other causes in 11.2% and idiopathic in 20.6%. All cases complained of chronic cough. The most common sign was daily sputum production (79.1%) and common symptoms were ral/crackle in 47.1% and wheezing in 25.4%. Mean treatment period was 32.82±11.56 months. At the end of follow-up, complete improvement occurred in 35.6%, partial improvement in 40.9% and no improvement in 23.5%. There was significant relation between existence of asthma ($p<0.001$), GERD ($p=0.02$) and CF ($p<0.001$) with response to treatment in bronchiectasis. The medication was used in 216 cases (57.8%) with antibiotics + seretide, 91 (24.3%) with antibiotics with fluoxetine + salmeterol, in 49 (13.1%) with antibiotics with serotide + anti-reflux and in 18 cases (4.8%) with antibiotics and serotide for the treatment of CF. In patients with and without the etiology of CF, the cure was observed in 1 (5.6%) and 132 (37.1%), partial remission in 5 (27.8%) and 148 (41.6%) of the cases and

non improvement in 12 (66.7%) and 76 (21.3%). This study demonstrated that cure and partial remission was statistically lower in CF patients (P<0.001) (Table.1).

Table 1: The efficacy of different treatments in regard of background etiology

Variables	Cure	Partial remission	Non improvement
Serotide	70 (32.45)	104 (48.1 %)	42 (19.5%)
Fluxetide + salmeterol	29 (31.9%)	33 (36.2%)	29 (31.9%)
Serotide + anti-reflux	33 (67.3%)	11 (22.4%)	5 (10.2%)
Serotide and CF treatment	1 (5.6%)	5 (27.8%)	12 (66.7%)

Discussion

Bronchiectasis is a chronic debilitating condition with considerable phenotypic diversity. A vicious cycle of infection and inflammation exists in damaged airways with patients suffering from persistent cough, purulent sputum production, recurrent chest infections and general malaise (15,16). The associated burden of disease in terms of increased morbidity, reduced quality of life and the socioeconomic cost of long-term management is significant. The most common cause of bronchiectasis is prolonged inflammation from repeated lung infections. Not everyone with cystic fibrosis will develop bronchiectasis, but about half of all people who have bronchiectasis also have cystic fibrosis (17,18). Bronchiectasis develops early in the course of cystic fibrosis, being detectable in infants as young as 10 weeks of age, and is persistent and progressive. Although the frequency of childhood bronchiectasis has been reduced in western countries, it remains a common problem in poorer countries and among certain demographic groups (19,20). In our study, in patients with and without the etiology of CF, the cure was observed in 1 (5.6%) and 132 (37.1%), partial remission in 5 (27.8%) and 148 (41.6%) of the cases and non improvement in 12 (66.7%) and 76 (21.3%). This study demonstrated that cure and partial remission was statistically lower in CF patients (P<0.001). In accordance to our study, Duff et al. demonstrated that in the patients with CF who had bronchiectasis cure rate was statistically lower than those who had bronchiectasis without the etiology of CF (21). In contrary to our study, Serisier et al. demonstrated that there was no statistically significant in patients with bronchiectasis with and without CF in regard of curing rate (22). There are multiple aetiologies for childhood bronchiectasis unrelated to cystic fibrosis. Some of these aetiologies, such as those predisposing to recurrent lung infections, e.g. immunodeficiencies, require treatment of the underlying condition and disease-specific pulmonary pathogens within the airway (23,24).

Regardless of aetiology, the treatments for bronchiectasis include antibiotics, airway clearance regimens, immunizations to prevent infections, and in some cases asthma therapies. The grade of evidence for specific treatments is low with few randomized controlled trials in children (25,26). Extrapolations of care provided to adults with bronchiectasis and patients with cystic fibrosis may not always be justified. Comprehensive care programs for children with bronchiectasis have demonstrated clinically relevant improvements over 2-7 years periods. Multi-center research is needed to rigorously evaluate current treatment practices for children with this disorder (27,28). In contrary to infant patients, bronchiectasis in patients with cystic fibrosis diagnosed in adulthood is

usually widespread, predominantly cylindrical, and is more severe in the upper lobes. The diagnosis of cystic fibrosis should be considered in adults with 'idiopathic' bronchiectasis showing these features on CT (29,30).

Conclusion

Bronchiectasis is common in infants with the etiology of CF and cure and partial remission is lower in CF patients who have bronchiectasis.

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