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ORIGINAL ARTICLE

Clinical and computed tomography findings of children with non-cystic fibrosis bronchiectasis seen in a pediatric pulmonology service

Danilo Santos Guerreiro[1], Vivianne Calheiros Chaves Gomes[1], Alexssandra Maia Alves[1], Claudia de Castro e Silva[1], Ana Julia Velozo Ribeiro[1]

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Abstract

Bronchiectasis is bronchial dilatation, usually diagnosed by chest tomography. Among the main causes are cystic fibrosis, infectious diseases and immunodeficiencies. In the pediatric age group there is a shortage of studies on non-cystic fibrosis bronchiectasis. We seek to describe epidemiological, clinical and etiological characteristics of children and adolescents with non-cystic fibrosis bronchiectasis accompanied in a pediatric Pneumology service. This is a cross-sectional, descriptive study of a sample of 72 patients under 18 years of age, followed up in the pediatric Pneumology service of a tertiary hospital linked to the Unified Health Sys-tem, reference in pediatrics for patients in the capital and in the interior of the state of Ceará The diagnosis was based on tomographic findings. There was a predominance of males (57%). Although the vast majority (90%) started symptoms before the age of 5, less than half (45%) were diagnosed with bronchiectasis before this age group. Almost all patients (97%) reported cough, 90% had expectoration and 80% reported dyspnea. All patients presented crepitations in the auscultation. The most frequently affected lobes were the lowest (23%) and the predominant classification was cylindrical (65%). Among the etiologies, 39% were of unidentified cause followed by post-infectious (28%) immunodeficiency (21%), probable primary ciliary dyskinesia (8%) and aspiration syndrome (4%). We concluded that despite the early onset of symptoms, there was a delay in the diagnosis of bronchiectasis. The proportion of unidentified and post-infectious causes was high. Greater investment is needed to expand diagnostic resources in reference centres.

[1] Albert Sabin Children's Hospital, Pulmonology Department - Fortaleza - Ceará - Brazil.

Correspondence to:
Danilo Santos Guerreiro.
Hospital Infantil Albert Sabin. Rua Tertuliano Sales, 544, Vila União, Fortaleza, CE, Brazil. CEP: 60410-794. E-mail: danilosg@hotmail.com

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INTRODUCTION

The term bronchiectasis refers to irreversible bronchial dilatation usually seen on CT scans of the chest[1,2]. It is clinically characterized by the presence of recurrent or persistent dry or productive cough associated with airway infection and inflammation[3]. Prevalence varies substantially (0.2-735 cases per 100,000 children). In recent years, prevalence has decreased in developed countries and increased in developing nations[1,4].

Bronchiectasis is one of the causes of chronic respiratory disease known for its high morbidity and mortality in low- and middle-income countries[5]. Bronchiectasis occurs mainly as a complication arising from infectious conditions such as pneumonia and tuberculosis, which are often seen in poorer populations.

At an individual level, bronchiectasis impairs the quality of life of patients and their caregivers and increases expenditure with healthcare[6].

The pathogenesis of bronchiectasis is multifactorial. The main accepted hypothesis is that there is a "vicious circle", in which an initial assault (viral and/or bacterial infection) on susceptible lungs (deficient innate and/or adaptive immune response) leads to airway inflammation, proteolysis, and oxidation with consequent hypersecretion of mucus and/or hyper-reactivity, thus impairing the mucociliary apparatus with increased susceptibility to infection and/or other injuries, leading to the development or worsening of bronchiectasis[7].

High-resolution computed tomography (HRCT) of the chest is the gold standard diagnostic method for bronchiectasis. It shows direct evidence of involvement such as bronchiolectasis, and indirect signs such as a mosaic attenuation pattern[2]. The definition of normal findings varies in the literature, with the broncho-arterial ratio ranging from >1 to 1.5 in adults and 0.8 in children[1].

Cystic fibrosis[8], immunodeficiency, ciliary dyskinesia, aspiration syndrome, congenital and obstructive syndromes[9] are the main underlying conditions causing bronchiectasis.

Infection is often polymicrobial with a predominance of Hemophilus influenzae, Streptococcus pneumoniae, and Moraxella catarrhalis. Differently from cystic fibrosis, other agents such as Staphylococcus aureus, Pseudomonas aeruginosa, Aspergillus, and nontuberculous mycobacteria are rarely seen in children[1].

Bronchiectasis requires multidisciplinary treatment involving physiotherapists, dietitians, nurses, and physicians. Drug therapy consists of antibiotics such as macrolides, quinolones, and beta-lactams. Influenza and pneumococcal vaccines must be prescribed and parents advised about the perils of second-hand smoking[1,3,9].

Given the diverse etiology and variable host characteristics, outcomes include mild involvement and fatal disease caused by airway obstruction, infection, and respiratory failure with hypercapnia. Bronchiectasis can be reversed with treatment in some cases, but children once diagnosed with the disease remain at high risk of developing new episodes and must be regularly followed up[9].

Few pediatric cases of non-cystic fibrosis bronchiectasis have been described in the literature. Management of the condition is based on data extrapolated from adult populations and patients with cystic fibrosis[10].

In view of the relevance of this subject to our reality, this article describes the clinical characteristics and imaging findings of children and adolescents with non-cystic fibrosis bronchiectasis followed-up in the pediatric pulmonology department of a tertiary referral hospital connected to the Brazilian Unified Healthcare System.

METHODS

This descriptive cross-sectional study involved the analysis of data from the medical records of a population of patients seen at the Pediatric Pulmonology Department of the largest pediatric referral hospital in Ceará, which is connected to the Brazilian Unified Healthcare System.

The following inclusion criteria were adopted: patients aged less than 18 years diagnosed with bronchiectasis based on high-resolution computed tomography (HRCT) scans of the chest, with a broncho-arterial ratio greater than or equal to 0.8, with or without the presence of indirect evidence of disease[1]. The presence of peribronchial thickening, low density nodules, mosaic attenuation, and mucoid impaction were considered indirect evidence of disease. Cystic fibrosis was ruled out based on diagnostic confirmation with the sweat test, with or without genetic testing. Diagnoses of bronchiolitis obliterans were based on clinical criteria (history of pneumonia or severe bronchiolitis) and CT scan changes consistent with small airways disease, after other potential conditions were ruled out. Probable primary ciliary dyskinesia was considered based on history of recurrent sinusitis/rhinitis/otitis, chronic productive cough in the first year of life, neonatal respiratory distress without apparent cause in full-term newborns, or laterality defect (situs inversus/ heterotaxy syndrome). Immunodeficiencies were diagnosed based on immunological tests and presence of aspiration syndromes derived from a history of frequent choking/regurgitation or global developmental delay. Cases of tuberculosis were diagnosed based on clinical criteria and positive smear tests and/or culture for Mycobacterium tuberculosis.

Data collection was performed by one of the authors in the period from January 2016 to December 2018.

We used a semi-structured questionnaire to capture the following variables: sex; age at diagnosis and onset of symptoms; clinical findings; etiology; type and location of bronchiectasis; number of CT scans performed during follow-up. Data were compiled in an Excel worksheet and further processed on statistical package StataCorp.

The hospital's Ethics Committee approved the study and granted it certificate no. 2.111.257.

RESULTS

Clinical and computed tomography findings

More than half (457%) of the 72 patients included in the study were males. Onset of symptoms occurred during the neonatal period in 22 patients (31%), during the first year of life in 23 (32%), between one and five years of age in 20 (28%), and after five years of age in seven (9%). The mean age at diagnosis of bronchiectasis was 7.4 years (range 1-17 years) and 32 (45%) were diagnosed before the age of five years (Table 1).

In terms of clinical findings, the most prevalent symptoms were cough in 70 patients (97%), followed by expectoration in 65 (90%), dyspnea in 58 (80%) and intermittent fever in 12 (16%). Hemoptysis was reported in only six cases (8%). On physical examination, all patients had crackles on pulmonary auscultation and 50 (60%) presented wheezing. Chest deformities were seen in 17 patients (24%) and digital clubbing in six (8%) (Table 1).

The cause of bronchiectasis was undefined in 28 patients (39%). Post-infectious causes were more frequent, with 20 patients (28%). Thirteen patients (18%) were diagnosed with bronchiolitis obliterans, five (7%) with post-tuberculosis bronchiectasis, and two (3%) with bronchiectasis secondary to pneumonia. Among other causes, 15 patients (21%) had immunodeficiency, six (8%) had probable primary ciliary dyskinesia, and three (4%) were diagnosed with aspiration syndrome (Table 2).

Regarding CT scan findings, 33 patients (65%) were diagnosed with cylindrical bronchiectasis, 16 (31%) with cystic disease, and two (4%) with saccular disease. In terms of location, the left and right lower lobes were affected in the same proportion, with 35 patients (23%). The middle lobe was the second most affected site with 34 cases (22%), followed by the lingula with 26 (17%), the right upper lobe with 17 (11%), and left upper lobe with three (2%). In most cases (65.3%) involvement was bilateral, encompassing more than two lobes, especially in bronchiectasis secondary to immunodeficiency (86.6%) and cases with an undefined etiology (60.7%). Middle and lower lobe involvement was present in all cases of probable primary ciliary dyskinesia. The lower lobes were involved in all cases of bronchiolitis obliterans, in 13 of 15 cases (87%) of immunodeficiency, and in 17 of 28 patients (61%) with disease with undefined causes (Table 3).

Table 1. Clinical characteristics.

Characteristics	n =72
Males, n (%)	41 (57)
Mean age at diagnosis of bronchiectasis (years)	7,4
Age at onset of symptoms	
Neonatal period - n (%)	22 (31)
> days and less than 1 year - n (%)	23 (32)
1-5 years - n (%)	20 (28)
>5 years - n (%)	7 (9)
Age at diagnosis of bronchiectasis	
< 1 year – n(%)	11 (15)
1-5 years - n (%)	21 (30)
>5 years - n (%)	40 (55)
Clinical findings	
Crackles - n (%)	72 (100)
Cough - n (%)	70 (97)
Expectoration- n (%)	65 (90)
Chest deformities - n (%)	58 (80)
Wheezing - n (%)	50(60)
Dyspnea - n (%)	17(19)
Intermittent fever- n (%)	12 (16)
Digital clubbing - n(%)	6 (8)
Hemoptysis - n (%)	6 (8)
Cyanosis - n (%)	2 (2)

DISCUSSION

There are few publications describing cases of non-cystic fibrosis bronchiectasis in children and adolescents.

This study describes the clinical and computed tomography findings of a population of patients seen at the Pediatric Pulmonology Outpatient Clinic of the Albert Sabin Children's Hospital, a member of the Brazilian Unified Healthcare System, located in Fortaleza, Ceará, Brazil. This is the largest pediatric referral hospital in the state of Ceará. The hospital provides care to patients with diseases of medium and high complexity referred from other centers in the state's capital and the countryside.

We found a slight predominance of males, as seen in other studies[11,12].

About 90% of the patients developed symptoms at a very early age. Unfortunately, the lack of diagnostic resources in our service did not allow the investigation of ciliary dyskinesia and some types of immunodeficiency. Access to advanced diagnostic methods has facilitated the diagnosis of these conditions[13]. In countries where consanguineous marriages are more prevalent and in which referral centers specialized in ciliary dyskinesia testing are available, primary ciliary dyskinesia has been pointed out as the main etiology for non-cystic fibrosis bronchiectasis in children[14].

On average, the patients included in our study were diagnosed with bronchiectasis at the age of seven years, as seen in other studies carried out in tertiary hospitals in low-, middle-, and high-income countries[12-16]. Diagnostic delays may be related to several factors, such as not considering the disease in differential diagnosis, poor access to referral centers, and scarcity of high-cost diagnostic tests.

Cough was present in almost all patients in our population (97%). The literature cites productive cough as the most frequent finding in individuals with bronchiectasis[11,16-18].

Table 2. Diagnosis of patients with bronchiectasis.

Cause	n =72
Undefined n (%)	28 (39)
Immunodeficiency n(%)	15 (21)
Bronchiolitis obliterans n (%)	13 (18)
Primary ciliary dyskinesia* - n (%)	6 (8)
Tuberculosis - n (%)	5 (7)
Pneumonia - n (%)	2 (3)
Aspiration syndrome	
Foreign body aspiration - n (%)	1 (1)
Dysphagia- n (%)	1(1)
Foreign body aspiration - n (%)	1(1)

*Probable diagnosis.

Chronic suppurative lung disease is characterized by persistent and productive cough and should serve as a warning sign in patients suspected with bronchiectasis, regardless of age, especially when associated with crackles on auscultation, a finding also present in all patients in our population.

In the last decade, the etiology of bronchiectasis has changed due to greater access to health services, early use of antimicrobials to control bacterial infections, and

Table 3. Bronchiectasis categorization and location.

Cause	n =72
Type	
Cylindrical - n (%)	33 (64)
Cystic - n (%)	16 (31)
Saccular - n (%)	2 (4)
Location	
Lower lobe* - n (%)	35 (23)
Middle lobe - n (%)	34 (22)
Lingula - n (%)	26 (17)
Upper right lobe	17 (11)
Upper left lobe	3 (2)
Laterality	
Unilateral n (%)	25(35)
Bilateral n (%)	47(65)

* Left and right lower lobes were equally involved.

improvements in vaccination coverage. As a result, post-infectious bronchiectasis has occurred due to other causes, especially in developed countries, where increased access to diagnostic resources has allowed genetic diseases including immunodeficiencies and dyskinesias to be diagnosed more frequently[13]. In our study, post-infectious causes predominated, with bronchiolitis obliterans topping the list. This is possibly due to the characteristics of the study population, which included mostly low-income individuals from a region with huge social disparities in a developing country.

Although this study was carried out in a tertiary referral hospital, tests for ciliary dyskinesia were not available, and a high proportion of the cases of bronchiectasis had an undefined etiology. The causes of bronchiectasis vary among studies[18-21] as does the proportion of cases with undefined etiology[22-25]. Several factors contribute to these differences, including the time and place in which the study was performed and the availability of diagnostic resources. The results of the present study indicate that more diagnostic resources are needed for patients with rare diseases.

Bronchiectasis is also categorized based on type and location. Cylindrical bronchiectasis predominated in our series, which might imply better outcomes in the medium and long term with proper management. The appearance of bronchiectasis varies with disease progression. Initially, cylindrical dilations of subsegmental bronchi are seen, which may later develop into saccular dilations. As the disease progresses, the bronchi become tortuous and start to be filled with mucopurulent and sometimes hemorrhagic material, which, if removed, reveals an edematous, necrotic, and frequently ulcerated mucosa, which can then develop into a cyst[9]. Although some authors have suggested that bronchiectasis may be reversed with early therapeutic measures[26,27], children with the condition must be regularly monitored, since they remain at high risk of developing new episodes of bronchiectasis[1].

Lower lobe involvement was predominant in our population. In the literature, bronchiectasis is more commonly seen in the lower lobes and preferentially affect the left lower lobe, probably because mucociliary clearance is impaired by the force of gravity[12-14]. The regional distribution of bronchiectasis correlates with some diseases. For example, lower lobe involvement is more common in primary ciliary dyskinesia, immunodeficiency, and aspiration syndrome. The upper lobes are preferentially affected in individuals with cystic fibrosis, while in nontuberculous mycobacteria infections, involvement of the middle lobe and lingula occurs more frequently[2,16,17].

The present study had other limitations. The data came from medical records, some of which with incomplete information, particularly in relation to the bacteriological profile of bronchiectasis, functional alterations, and quality of life.

Although the study was conducted at a referral center, diagnostic delays affected all patients with bronchiectasis. Moreover, a substantial proportion of the cases of disease were attributed undefined of post-infectious causes. Investments are needed to expand the diagnostic capabilities of referral centers in Brazil. Specific protocols for diagnostic investigation, treatment, and follow-up of pediatric patients with bronchiectasis must be developed and adapted to our reality. The identification of modifiable risk factors will also allow the introduction of measures for the prevention and early treatment of children with respiratory infections.

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