

Non-Cystic Fibrosis Bronchiectasis in Children: Diagnosis and Management

Marcella Gallucci*, Emanuela di Palmo and Giampaolo Ricci

Pediatric Unit, Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy

***Corresponding Author:** Marcella Gallucci, Pediatric Unit, Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy.

Received: October 26, 2016; **Published:** November 08, 2016

Abstract

Bronchiectasis is a heterogeneous disease associated with significant morbidity in children. The real incidence is unknown and the prevalence is increased in developing countries and lower socioeconomics classes. The most common association in children is a previous pneumonia and most frequent symptom is chronic and often productive cough. The use of high-resolution computed tomography (HRCT) has improved the time of diagnosis allowing earlier treatment. In children, the term "bronchiectasis" must be used with prudence seeing as how some HRCT changes can to improve or resolve. Promising is the use of chest magnetic resonance imaging (MRI) as a radiation-free technique for the assessment and follow-up of lung abnormalities in non-Fibrosis Cystic chronic lung disease. NCFB management need of a multi-disciplinary care and the cornerstones of treatment are antibiotics and chest physiotherapy (CPT) even if guidelines in children are lacking. The Azithromycin because of its anti-inflammatory effects and its direct antimicrobial effect on Gram positive cocci could be a new option for prevention of exacerbation in non-cystic fibrosis bronchiectasis.

Keywords: *Bronchiectasis; Children; Chronic and Productive Cough; HRCT; Antibiotics; Azithromycin; Chest Physiotherapy (CPT)*

Abbreviations

NCFB: Non-Cystic Fibrosis Bronchiectasis; HRCT: High-Resolution Computerized Tomography; MRI: Magnetic Resonance Imaging; CPT: Chest Physiotherapy

Introduction

Non-cystic fibrosis bronchiectasis (NCFB) is a chronic pulmonary disorder characterized by irreversible and usually progressive dilatation of one or more bronchi, due to structural modification in the bronchial wall and chronic inflammation of the airway. Historically bronchiectasis has been described as cylindrical, varicose or cystic as defined by bronchography and these characterizations respectively seems correlates with increasing degree of severity [1].

Excluding Cystic fibrosis, recurrent pneumonia is one of the most frequent causes of children bronchiectasis; others factors includes primary immune deficiencies, primary ciliary dyskinesia, foreign body aspiration but also structural airway abnormalities such as bronchomalacia and congenital tracheobronchomegaly (Table 1) [2]. NCFB in children usually presents with chronic respiratory symptoms. Cough with daily sputum production is the most common clinical presentation and may be present for years before diagnosis. Recurrent wheezing dyspnea, hemoptysis and delayed growth are additional findings [3,4]. Recurrent pulmonary exacerbations are associated with progressive decline of lung function.

<p style="text-align: center;">CFTR mutations</p> <p style="text-align: center;">- Cystic fibrosis classic and atypical</p>
<p style="text-align: center;">Disregulated immune function:</p> <p style="text-align: center;">Primary immune-deficiencies X-linked A gamma globulinemia Common variable immunodeficiency (CVID) HIES or STAT3 deficiency</p>
<p style="text-align: center;">Primary Ciliary Dyskinesia</p> <p style="text-align: center;">PCD, Kartagener Syndrome</p>
<p style="text-align: center;">Infections</p>
<p style="text-align: center;">Structural congenital malformation:</p> <p style="text-align: center;">Congenital tracheo-bronchomegaly (Mounier-Kuhn syndrome, William-Campbell syndrome) Congenital lobar emphysema</p>
<p style="text-align: center;">Bronchial obstruction</p> <p style="text-align: center;">Inhaled foreign body Tumor Mycobacterium</p>
<p style="text-align: center;">Associated conditions</p> <p style="text-align: center;">Recurrent aspiration secondary to neuromuscular disorders Tracheo-esophageal fistula or gastro-esophageal reflux</p>

Table 1: Most frequent conditions associated with children Bronchiectasis.

Diagnosis

In children, no standardized method of classification severity has been defined, even if clinical, radiographic and microbiologic finding are usually used for quantifying bronchiectasis severity [5].

However, a radiological diagnosis of bronchiectasis in children should be considered with caution because of has been showed in some cases a complete radiological resolution of bronchial dilatation after medical treatment [6].

Chest radiography in children has a poor diagnostic value for bronchiectasis, so a suggestive clinical history should prompt additional investigation.

High-resolution computerized tomography (HRCT) with 1.5 - 3 mm collimation is the imaging method of choice. HCRT finding include bronchial dilatation, bronchial wall thickening, lack of normal bronchial tapering or any bronchi with an internal diameter greater than the diameter of the accompanying pulmonary artery and bronchi visible closer than two centimeters to the pleural surface. The distribution of abnormalities on HRCT is not necessarily linked to etiology [7].

Recently chest magnetic resonance imaging (MRI) has been proposed as a radiation-free technique for the assessment and follow-up of several chest disorders; especially high-field 3.0 -T MRI showed a good agreement with HCRT for detection of several abnormalities such as peri-bronchial wall thickening, mucous plugging and collapse/consolidation [8].

Spirometry may be useful in determining disease severity in older children and can to reveal either an obstructive or mixed obstructive/restrictive airflow pattern. Other test as measuring static lung volumes and the 6 min walk test can be used for assessing functional impairment [9].

Bronchoscopy is helpful in identifying underlying structural anomalies and obtaining lower airway secretions from children unable to expectorate [10]. The determination in exhaled breath condensate of metalloproteases (MMP-9) could be a useful marker of airway injury in patients with NCFB [11].

Management

NCFB management need of a multi-disciplinary care with the aim of controlling symptoms, reduce exacerbations and preserved lung function.

The cornerstones of therapy are antibiotics and chest physiotherapy (CPT) even if guidelines in children are lacking.

Antibiotics must be used to treat acute exacerbations or as prophylaxis treatment to reduce rates of exacerbations. The use and choice of antibiotics must be led by sputum samples or cough swab and when it possible by bronchoalveolar lavage culture. In children bacterium, often isolated are non-encapsulate *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Staphylococcus aureus*. Infection with *Pseudomonas aeruginosa* is more infrequent in children and can be associated to underlying diseases with increasing lung damage [12].

Prolonged antibiotic therapy (more than 4 weeks) are often necessary to eradicate some respiratory pathogens [13]. At present, there are no randomized controlled trials (RCTs) evaluating the efficacy of inhaled antibiotics in children with NCFB, even if this option has been widely used and showed numerous benefits [14].

In the last years, there is an increased interest in macrolides for the therapy of NCFB because of their anti-inflammatory effects and its well established direct antimicrobial effect on Gram positive cocci and atypical pathogens but also for the properties to decrease mucus production.

Two meta-analyses that included seven studies evaluating various macrolides (azithromycin, erythromycin, roxithromycin) reported a decreased rates of exacerbation compared with placebo [15,16].

A randomized double-blind trial of New Zealand showed that the use of Azithromycin three times a week for 6 months in patients with NCFB significantly decreased the rate of event-based exacerbations and increases the time to the first event-based exacerbation compared with placebo [17].

Chest physiotherapy (CPT) is usually recommended in children with bronchiectasis even if evidences in support of these practice are lacking and principally descends from study on CF.

The application of positive expiratory devices and high-frequency chest wall oscillation showed an improvement of FEV1 as indices of lung function [18].

Also, inhaled mannitol seems to improve the quality of life even if did not reduce exacerbation rates [19].

A Cochrane review of mucolytic agents reported a positive effects of recombinant DNase in patient with NCFB [20].

A Cochrane systematic reviews of randomized controlled trials of combined ICS and LABA compared with control in children and adults with NCFB founded that the first strategy was marginally better than high-dose ICS in improving clinical symptoms like cough free-day but showed no significant improvement in rates of exacerbations and no change in lung function indices [21]. So more robust evidence is necessary to make any significant recommendations of their routinely use in non-CF bronchiectasis.

Conclusions

The most common cause of NCFB include infections, immunodeficiency, aspiration and primary ciliary dyskinesia. An early diagnosis is essential to prevent progressive decline of lung function.

The use of HRCT is the gold standard to confirm bronchiectasis but magnetic resonance imaging (MRI) could be promising as a radiation-free technique for the follow-up.

Actually, the keystone of treatment is specific antibiotic therapy for the different pathogen in association with chest physiotherapy. Often is essential long-term antibiotics to decrease the bacterial load.

Inhaled antibiotics, inhaled mannitol, mucolytic agents and combined ICS and LABA can be useful in improving the quality of life.

At last Azithromycin seems to decrease the rate of event-based exacerbations and increases the time to the first event-based exacerbation compared with placebo and so can be a precious option in NCFB management.

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Volume 2 Issue 5 November 2016

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