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CASE REPORT

Resolution of bronchiectasis in 3 children. Case series description

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ABSTRACT

Bronchiectasis is a chronic disease syndrome manifested by a productive cough, subsequent to structural changes in the bronchial walls resulting from bacterial infection and leading to the retention of secretions. In some patients, the cause of bronchiectasis is chronic diseases, such as cystic fibrosis, ciliary dyskinesia, α1-antitrypsin deficiency, or congenital immune disorders. However, there are cases of bronchiectasis without underlying chronic disease, e.g. as a consequence of severe lower respiratory tract infection (bacterial or viral) or local airway obstruction, caused by foreign body aspiration or external pressure. Currently, it is believed that in some patients bronchial deformations may be reversible with a sufficiently quick diagnosis and implementation of treatment. The paper presents the cases of 3 children in whom the resolution of dilated lesions was confirmed by computed tomography.

KEY WORDS:

computed tomography, bronchiectasis, chronic inflammation.

INTRODUCTION

Bronchiectasis is a disease syndrome manifesting with a chronic, productive cough. Chronic inflammation and bacterial infection persist in the lower airways, and changes in the form of dilatation and distortion of the bronchi are found on high-resolution computed tomography (HRCT) (which is the basis for diagnosis). The disease is relatively rarely diagnosed in children [1], and the prevalence in Western Europe is estimated at around 0.5–2.3/100,000 [2].

In the original definitions, also used in the twenty-first century, bronchiectasis was defined as irreversible changes, present throughout the life of the patient [1, 3, 4]. However, since the end of the 20th century, there have been several publications documenting the possibility of regression of dilated lesions. The paper by Eastham *et al*. was one of the first, describing in 2004 the resolution of lesions in 18 out of 93 observed patients with bronchiectasis diagnosed at the age of 1.6–18.8 years. In the described patients, the radiological changes in HRCT regressed within 18 months of diagnosis [5]. In relation to similar reports, it is currently assumed that in some cases – with timely diagnosis and implementation of treatment – it may be a reversible process [6].

Due to the complex etiology, after the diagnosis of bronchiectasis, it is necessary to extend the diagnostics in order to determine the cause of the disease, which may allow for possible causal treatment in selected patients. In some patients, the cause of bronchiectasis may be chronic diseases associated with disorders of mucociliary clearance (such as cystic fibrosis or ciliary dyskinesia) or increased susceptibility to infections (e.g. α1-antitrypsin deficiency, congenital immune disorders) [7, 8]. However, up to half of the children with bronchiectasis have developed this syndrome without the presence of underlying chronic disease. The development of bronchiectasis may be a consequence of a severe infection of the lower respiratory tract or local disorders of bronchial patency (through endobronchial blockage, e.g. a foreign body or

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external pressure). In about a third, the potential mechanism (idiopathic dilation) cannot be determined.

The chance of resolution of bronchiectasis varies depending on the etiology, time to onset (and diagnosis), and treatment. Recurrent and especially chronic lower respiratory tract infections (e.g. chronic bacterial bronchitis) are a significant risk factor for the development of bronchiectasis [9].

With appropriate management, early post-infectious bronchiectasis in children and adolescents can be reversible, with resolution or improvement rates as high as approximately 60% [6].

The aim of the study was to present the resolution of bronchiectasis in three children, which was documented by HRCT.

CASE REPORTS

CASE 1

A 10.5-year-old girl was hospitalized due to auscultatory changes persisting in both lungs. So far, she had not been ill often, and the course of the infection was typical for her age. About 4 months before admission, she had an infection with an isolated wet cough, without auscultatory changes at the time. Clarithromycin and nebulization with steroids and bronchodilators were used in the treatment, resulting in improvement of the general condition and resolution of cough. After about a month, the symptoms recurred, but despite repeated antibiotic therapy with macrolides and mucolytic nebulization, the productive cough persisted until hospitalization, i.e. for over 2 months. In addition, a slightly reduced exercise capacity was noted.

On admission, the patient was in good condition. On auscultation over the lungs bilateral crackles and mid-bubble rales were found. Laboratory tests revealed no significant abnormalities. Skin tests showed a positive result for allergens of house dust mites (3 mm, 4 mm) and grass pollen (3 mm). Sweat chloride levels were normally low, as well as the concentration of nitric oxide in exhaled air (fractional exhaled nitric oxide [FeNO]; through the mouth and nose). In the body plethysmography, airway resistances and flows were normal. The bronchoscopy revealed a large amount of purulent secretions in the trachea and bronchi of both lungs, with the largest amount in both lower lobes. After aspiration of the secretion, swelling, and redness of the mucous membranes were observed. The culture of the bronchial content showed an increased amount of the physiological flora only, but the cytological assessment revealed more than 25 neutrophils and several eosinophils in the visual field. High-resolution computed tomography showed thickening of the walls and bronchiectasis of both lower lobes and discrete bronchiectasis of the left segment 4. The diagnosis of bronchiectasis and the suspicion of eosinophilic bronchitis were established.

For about half a year after the diagnosis, auscultatory changes persisted and exacerbations requiring antibiotic treatment occurred several times. During the period of increased productive cough, inhalation and physiotherapy were implemented. In addition, in the autumn and winter seasons, azithromycin in an anti-inflammatory dose was administered (a total of about 12 months of therapy) and inhalation of budesonide. Over the years, exacerbations were less frequent and of shorter duration. Inflammation markers were low at all eight control visits. No bronchial obstruction was found in lung function tests (at first hospitalization forced expiratory volume [FEV_1] 92% of predicted, forced vital capacity [FVC] 92% of predicted, FEV_1/FVC 88.52%, last hospitalization FEV_1 93% of predicted, FVC 84% of predicted, FEV_1/FVC 99.22%), and no wheezing was observed. Sputum examinations showed multiple neutrophils (four times, > 25 high power fields [HPF]) and several eosinophils (twice, 5–10 HPF). In each case, sputum cultures showed only an increase in the natural flora of the respiratory tract. During the last few stays, the patient failed to cough up sputum, so cytological analysis of the sputum could not be performed. Four years after the diagnosis, no auscultatory changes were found, and the HRCT image of the bronchial tree was normal (Figure 1).

CASE 2

A 15.5-year-old boy was admitted due to recurrent, prolonged bronchitis with concomitant rhinitis. The pa-

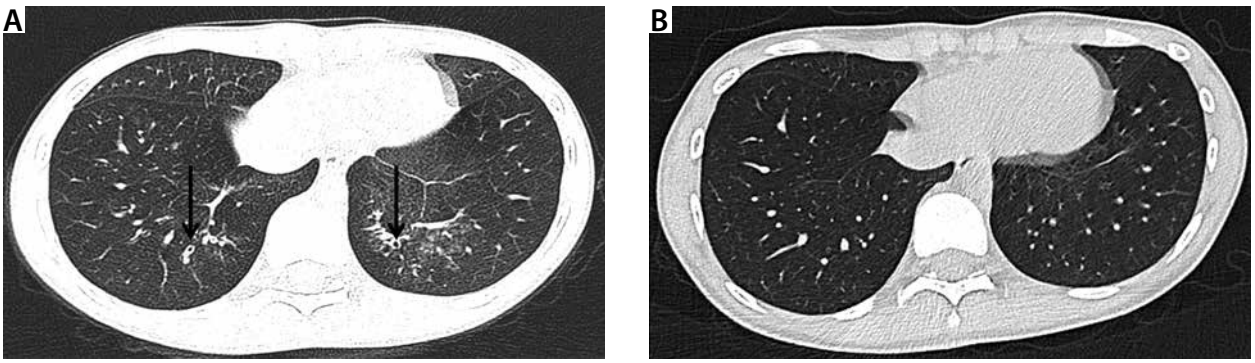

FIGURE 1. On the left side high-resolution computed tomography (HRCT) with bronchiectasis from 2018, on the right side HRCT without bronchiectasis from 2022

tient did not have a chronic cough; this symptom was present only during infections, which lasted about 4 weeks.

On admission, the patient was in good condition, with a normal alveolar murmur on auscultation over the lungs. Laboratory tests showed a slightly elevated concentration of total IgE (199 IU/ml). Induced sputum cytology showed neutrophils (> 25 HPF) and eosinophils (0–5 HPF). Normally low sweat chloride levels ruled out cystic fibrosis. Skin prick tests showed small reactions to house dust mites (2.5 mm) and grass pollen (2.5 mm). In the spirometry, the patency of the bronchi was normal and the FeNO value in the air exhaled through the mouth was borderline (23.5 ppb). Fractional exhaled nitric oxide in the air exhaled through the nose was normally high, and cough and rhinitis were not present from the first years of life, so we excluded the syndrome of primary ciliary dyskinesia. High-resolution computed tomography of the chest showed small bronchiectases in the lower lobes of both lungs. Bronchiectasis and chronic rhinitis were diagnosed. Chronic treatment was recommended with a nasal steroid, and in periods of exacerbation, physiotherapy and mucolytic nebulization.

During the second hospitalization, the nitric oxide in the air exhaled through the mouth was elevated (59.1 ppb), and inhaled glucocorticosteroids were used for 5 months due to the suspicion of bronchial asthma. Sputum neutrophilia occurred on one more sputum examination, but eosinophilia did not recur on two subsequent follow-up examinations. Over time, lower respiratory tract infections became less frequent and milder, and only natural respiratory tract flora was found in cultures. There were no audible wheezes during any of the four follow-up examinations, and spirometry consistently showed no signs of bronchial obstruction (first hospitalization FEV_1 130.9% of predicted, FVC 128% of predicted, FEV_1/FVC 84.95%, last hospitalization FEV_1 139% of predicted, FVC 134.8% of predicted, FEV_1/FVC 85.59%). In skin tests (repeated twice) a small reaction to mite allergens was maintained (4 mm after 2 years). The follow-up HRCT performed after two years showed a normal image of the bronchial tree (Figure 2).

CASE 3

A 10-year-old girl was admitted due to a productive cough and persistent auscultatory changes. These symptoms started after pneumonia 5 months ago and were treated with antibiotics (macrolides, amoxicillin with clavulanic acid) without improvement.

On admission, she was in good general condition. On auscultation, rales were present over the lung fields, predominantly on the left side at the base. Laboratory tests revealed a slightly accelerated erythrocyte sedimentation rate (14 mm/h), positive IgG for *Chlamydophila pneumoniae*, *Bordetella pertussis*, and Epstein-Barr virus. High-resolution computed tomography of the chest showed bronchiectasis in the lower lobe of the left lung, as well as in the middle and lower lobes of the right lung. In sputum cytology, neutrophils (> 25 HPF) and a few eosinophils (0–4 HPF) were present, but no growth of pathogenic flora was found. Systematic inhalation with mucolytic or hypertonic saline , physiotherapy, and azithromycin in an anti-inflammatory dose were recommended.

During the second hospitalization after 6 months, eosinophils in the sputum accounted for 8%, which, in the absence of typical asthma symptoms and normal spirometry, allowed the diagnosis of eosinophilic bronchitis. Inhaled budesonide was added to the treatment. Over time, exacerbations became less frequent and milder. The patient was hospitalized four times in total, and no pathogenic bacteria were found in each sputum culture. Allergological tests until the last visit were negative, and no bronchial obstruction was found in spirometry (first hospitalization FEV_1 81% of predicted, FVC 90% of predicted, FEV_1/FVC 78.28%, last hospitalization FEV_1 97% of predicted, FVC 100% of predicted, FEV_1/FVC 85.80%). In the follow-up HRCT, performed more than four years after the diagnosis, a normal picture of the bronchial tree was found (Figure 3).

CONCLUSIONS

In the three described children, the resolution of bronchiectasis, demonstrated by HRCT, was docu-

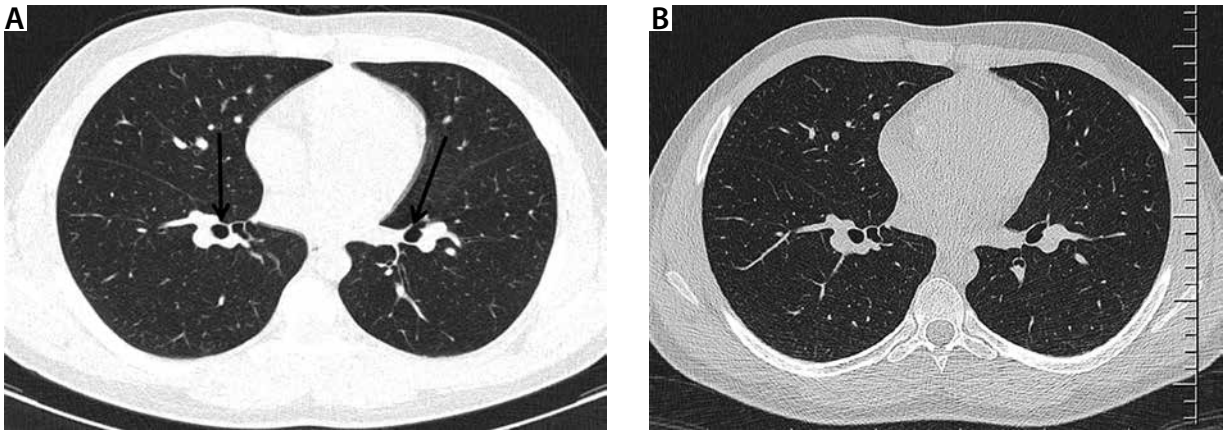

FIGURE 2. On the left side high-resolution computed tomography (HRCT) with bronchiectasis from 2011, on the right side HRCT without bronchiectasis from 2013

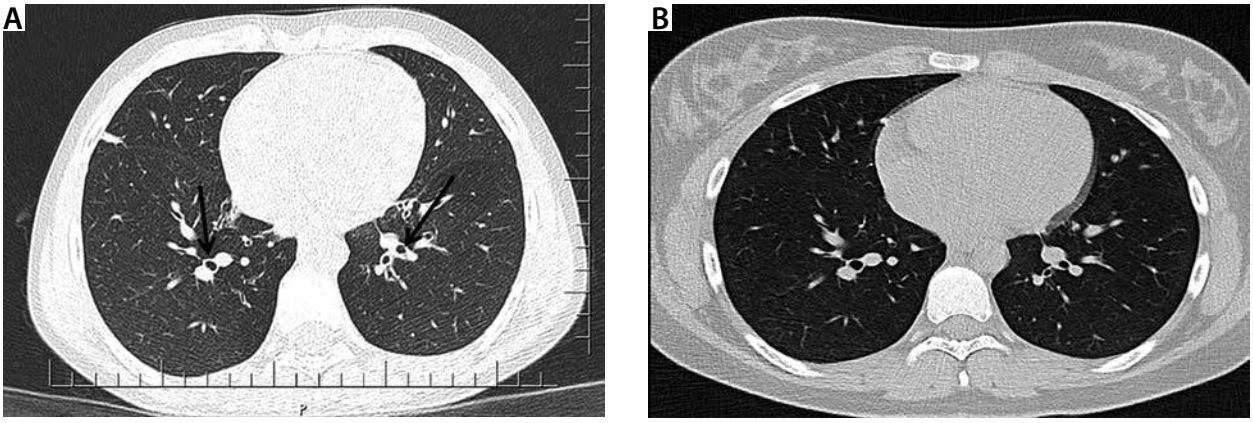

FIGURE 3. On the left side high-resolution computed tomography (HRCT) with bronchiectasis from 2018, on the right side HRCT without bronchiectasis from 2022

mented. Increased neutrophil counts were observed in sputum in initial studies, but no lower respiratory tract bacterial pathogens associated with bronchiectasis were found in any of the children presented.

According to current views, a vicious circle of infections, chronic inflammation, and lower respiratory tract obstruction plays a key role in the development of bronchiectasis, leading to the destruction of the bronchial walls according to Cole's hypothesis [10]. It is assumed that early treatment, allowing the vicious circle to be broken, may lead to the inhibition and resolution of chronic inflammation, ultimately making it possible to reverse the changes meeting the criteria for bronchiectasis [6].

In accordance with the guidelines [6], in all 3 children high-resolution CT was used to diagnose bronchiectasis. After that, the main underlying diseases were ruled out. Once the diagnosis was established, regular airway clearance techniques were used, with mucoactive agents used only periodically. All children were reviewed regularly to monitor the course of the disease. Finally, chest CT scans were repeated to determine whether this management was still necessary.

It is worth emphasizing that the current guidelines of the European Respiratory Society suggest that in children (unlike in adults) the borderline value of the BAR index (broncho-arterial ratio, defined by the ratio of the inner diameter of the airway to the outer diameter of the adjacent artery) indicating bronchiectasis should be taken as > 0.8 and not so far > 1–1.5. This will increase the diagnosis of the disease and allow for faster implementation of treatment, creating in some cases a chance for the lesions to subside. However, this may lead to overdiagnosis, so it is important to order imaging tests based on the clinical picture (in particular, chronic productive cough) suggestive of bronchiectasis.

In the described children, both CT examinations were performed several months after the last lower respiratory tract infection, which could have initiated a chain of events leading to the development of bronchiectasis. Avoiding CT shortly after acute lower respiratory tract infection is suggested to reduce the risk of overdiagnosis of dilatation. Prolonged pulmonary vasoconstriction in hypoxic areas (e.g. as a consequence of atelectasis resulting from surfactant deficiency due to damage to type II pneumocytes in the course of acute infection of the lung parenchyma) may lead to transient thinning of the bronchial wall. This may lead to an increase in BAR and result in overdiagnosis of bronchiectasis [11]. Therefore, premature chest CT early after lower respiratory tract infection may reveal transient changes, which are a consequence of inflammation, and gradually disappear with recovery [12].

An example of the importance of early intervention is the well-known relationship between the time from aspiration of a foreign body to its removal and the development of bronchiectasis. Foreign bodies of organic origin and time over 30 days are the most important factors in the development of bronchiectasis [13]. In the case of foreign body aspiration, it is, therefore, crucial to perform a bronchoscopy as soon as possible to avoid long-term consequences [14]. There are suggestions that reversibility of bronchial damage is also possible in the case of some systemic diseases, provided that the defect of the underlying disorder can be corrected. Baris and colleagues reported the resolution of dilated lesions in 3 out of 12 patients with common variable immunodeficiency (CVID) after treatment with IVIG [15], confirming the possibility of slowing or preventing disease progression with appropriate treatment [15, 16].

In all the presented children, after the diagnosis of bronchiectasis, symptomatic management was implemented, which included physiotherapy and, periodically, nebulization of mucoactive drugs (hypertonic NaCl or ambroxol). During the period of productive cough, airway cleansing (bronchial toilet) could prevent the development of chronic inflammation in deformed bronchi, which favored the reconstruction of the bronchial structure. However, in the ERS guidelines, the use of mucoactive drugs (i.e. bromhexine, dornase, hypertonic saline nebulization) is not recommended routinely [6], but only in patients with severe symptoms who have difficulty coughing up sputum [6, 17]. Recent publications confirm the beneficial effect of nebulization with hypertonic salt. Anuradha *et al.* [18] in a group of 52 children with bronchiectasis in a cross-over trial observed an improvement

in spirometric indices during the use of 3% NaCl nebulization compared to salbutamol alone.

It is recommended that an exacerbation of bronchiectasis be recognized as ≥ 3 days of worsening respiratory symptoms, mainly cough (with or without increased sputum), except in immunocompromised patients or dyspnea, in which case treatment should be initiated immediately [6]. Antibiotic therapy should be used for 14 days. Empirically, amoxicillin-clavulanate is the antibiotic of first choice, but treatment should be based on sputum culture [6].

None of these patients had a chronic disease or identifiable cause that could lead to the development of dilatation. The probable cause of bronchiectasis could be damage to the structure of the bronchi, induced by a lower respiratory tract infection. It is worth emphasizing that no growth of pathogenic bacteria was observed in sputum tests. This cannot be explained by age-specific difficulties in obtaining sputum in children, as it was obtained in 12 out of 17 examinations performed in a total of 3 children. The absence of bacterial pathogens typically found in bronchiectasis (e.g. *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*) may indirectly confirm the post-infectious nature of bronchiectasis, and the absence of chronic bacterial infection may have facilitated the reconstruction of the normal bronchial structure. The age of patients entering puberty, associated with rapid body development, could also play a role.

In the three described children, the role of transient sputum eosinophilia, as well as the use of inhaled corticosteroids (ICS), is not clear. All patients were temporarily treated with inhaled glucocorticosteroids due to the suspicion of eosinophilic bronchitis. Although the role of neutrophilic inflammation in the development of bronchiectasis has been classically assumed so far [19], the role of eosinophilic inflammation may be greater than previously assumed. Up to 20% of adult patients with BE may have eosinophilic inflammation [20–22]. A greater improvement in the quality of life after ICS administration was also demonstrated in patients with bronchiectasis and sputum (> 3%) or blood (> 150 cells/μl) eosinophilia [23]. Routine use of ICS in patients with dilations is not recommended, however, because there is insufficient evidence for the benefits of ICS in all patients with bronchiectasis [24]. Their chronic use promotes adrenal suppression and increases the risk of pneumonia [6].

In both girls, in addition to standard treatment, azithromycin in an anti-inflammatory dose was also used periodically, which could have had a positive effect on the frequency of exacerbations. Chronic use of azithromycin is currently recommended in selected patients with bronchiectasis [6, 25] – who have had at least three outpatient exacerbations or one requiring hospitalization in the last 12 months [6].

In summary, the resolution of the dilated lesions was documented in the three presented cases. Potential indicators of resolution could be the absence of chronic inflammation and pathogens in the sputum. Nevertheless, these examples suggest that it is worth paying attention to a quick reaction in the case of symptoms indicating a chronic infection of the lower respiratory tract. Greater awareness of the importance of early intervention for prolonged lower respiratory tract symptoms may contribute to a reduction in the rate of bronchiectasis [6, 15, 16, 26, 27].

DISCLOSURE

The authors declare no conflict of interest.

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