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Are airways structural abnormalities more frequent in children with recurrent lower respiratory tract infections?

Mikel Santiago-Burruchaga [a,*], Rafael Zalacain-Jorge [b], Carlos Vazquez-Cordero [a]

[a] *Paediatric Pulmonology Unit, Paediatric Department, Spain*
[b] *Pulmonology Department, Spain*

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Summary
We report bronchoscopic changes observed in children with recurrent lower airways infections (RLAI) and findings in control children undergoing bronchoscopy for causes other than RLAI.
Patients and methods: Retrospective case-control cohorts study. The clinical records of children who had fiberoptic bronchoscopy (FB) for a history of RLAI without any known underlying disorder between 2007 and 2013 and of control children who required FB for other causes were reviewed. Clinical features, bronchospic findings and bronchoalveolar lavage (BAL) results were assessed.
Results: Cases were 62 (32 female) children aged 5 years (1–12) and controls 29 children aged 4.5 years (0.5–14). Airway malacia was observed in 32 (52%) vs 4 (13%) ($p = 0.001$), profuse respiratory secretions in 34(55%) vs 6 (20%) ($p = 0.007$). Endobronchial obstruction: 4 (6.4%) and tracheobronchomegaly were observed only in cases. In cases with profuse respiratory secretions there was a higher prevalence of airways malacia: 64.7% vs 35.7% ($p = 0.04$) and of positive BAL cultures: 45.5% vs 13.3% ($p = 0.04$). Isolated organisms in cases were non-typable *Haemophilus influenzae* and *Streptococcus pneumoniae* most frequently. *Pneumocystiis jirovecii*, *Staphylococcus aureus*, and *Streptococcus mitis* were isolated in controls.
Conclusions: Half of the children with RLAI had tracheo and/or bronchomalacia, their frequency being in keeping with previous reports and far higher than that observed in controls. It was associated with profuse respiratory secretions and with a higher frequency of positive BAL cultures mostly for non typable *H. influenzae* and *S. pneumoniae* which were not isolated in controls.

* Corresponding author. Hospital Universitario de Cruces, Plaza de Cruces s/n, 48903 Barakaldo, Bizkaia, Basque Country, Spain. Tel.: +34 946006485.
E-mail addresses: MIKEL.SANTIAGOBURRUCHAGA@osakidetza.net (M. Santiago-Burruchaga), RAFAEL.ZALACAINJORGE@osakidetza.net (R. Zalacain-Jorge), CARLOS.VAZQUEZCORDERO@osakidetza.net (C. Vazquez-Cordero).

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Introduction

Recurrent lower airways infections involve the pulmonary parenchyma and or the lower airways. Although the scope of the term can greatly vary depending on the kind and number of episodes that are included, their incidence in childhood has been estimated to be about 7% [1]. Their clinical presentation ranges from episodes of persistent bacterial bronchitis (PBB) and or recurrent pneumonia, to chronic suppurative pulmonary disease with or without bronchiectasis [2]. Inflammation-infection vicious circles, and colonization of the lower airways with organisms coming from the upper airways, owing to disturbed mucociliary clearance are thought to underlie their pathogenesis [3]. Disturbed mucociliary clearance is generally secondary to viral infections and inflammatory damage, but occasionally is caused by congenital conditions (cystic fibrosis, primary ciliary dyskinesia, inmunodeficiency…). Once non-invasive approaches to diagnosis have failed, FB is often considered for cases with either severe or protracted symptoms and in patients with associated conditions, in order to obtain biological samples and to rule out airways structural abnormalities. Airways malacia is a structural and functional weakness of the tracheal and/or bronchial walls due to cartilaginous rings abnormalities, or increase in the length of the posterior fibromuscular walls. It gives rise to complete or partial dynamic collapse of the airways lumen, hampering cough effectiveness and interfering with mucociliary clearance, leading to plugging of the airways with bronchial secretions [4]. While the incidence of malacia has been reported to be 1 in 2100 newborns [5], it is probably higher among children with RLAI [6–8]. The scarcity of reports of bronchoscopic findings in control healthy children because of the ethical problems of performing an invasive procedure in such a population prevents comparing their incidence of malacia with that found in children with RLAI. The aim of our study was to describe the bronchoscopic changes in children with RLAI, to investigate the prevalence of lower airways malacia as compared with previous reports, and to assess their prevalence in a control group of children having bronchoscopy for causes other than RLAI.

Patients and methods

Retrospective case–control cohorts study. The clinical features, bronchoscopic findings and the BAL results of children referred for FB for a history of RLAI between 2007 and 2013, and of control children who required FB for other causes were assessed.

Patients were considered to have RLAI if they had any of the following: recurrent pneumonia (2 or more in a year or 3 or more at any time), chronic wet or productive cough for over 4 weeks, persistent atelectasis (for over 3 months), or bronchiectasis (bonchial/arterial diameter ratio over 1–1.5 on chest CT scans). Children with associated conditions such as bronchopulmonary dysplasia, prematurity, difficult to control asthma, cystic fibrosis, immunodeficiency, genetic syndromes, neuromuscular, CNS or heart disease, airways or digestive tract malformations, severe scoliosis, protracted endotracheal intubation, tracheotomia or endobronchial aspiration syndromes were excluded. A control group of children without a history of RLAI who had FB for other causes over the same time span and fulfilled the same exclusion criteria were also studied. Age, sex, clinical presentation, duration of the symptoms, FB/BAL results and final diagnosis were all recorded.

FB (Olympus videobronchoscope) were performed at the Pediatric Intensive Care Unit on spontaneous breathing under sedation-analgesia and local anesthesia. Images were video recorded and reviewed later. BAL was performed at either the right middle or right lower lobes, by infusing and suctioning 0.9% saline. Recovered samples were shipped to the laboratory and studied according to the microbiology&pathology BAL protocol followed in our Hospital. A CFU count over 10^4 was considered as consistent with bronchopulmonary infection. Any growth of normal oropharyngeal organisms was disregarded. Airways malacia was considered to be present in the face of an over 50% dynamic collapse of the airways lumen during expiration on spontaneous breathing or during cough, while no suctioning was being applied [8]. Its severity was classified as mild if $<$ 70%, moderate if $\geq$ 70 $<$ 90% and severe if $\geq$ 90%. Bronchial stenosis was diagnosed when bronchial opening was either absent or severely decreased after applying mild suctioning as compared with that observed in neighboring bronchi. An observed increased amount of respiratory secretions was the only change considered to be consistent with bronchitis.

Statistics were performed by using SPSS software for Windows, version 11,0 (SPSS Inc., Chicago, IL, USA). Numeric variables were expressed as medians and the distribution of category variables as frequencies and percentages. Differences between groups were assessed using Chi square, Student t, and Mann Whitney analysis. A p value <0.05 was considered to be significant.

Results

Cases were 62 children (34 female) [aged 60.5 months (12–144)]. Sixty (96.6%) were scheduled for FB from our outpatient clinic [twenty-eight (45%) had been seen previously at four different Pediatric Chest Medicine Hospital Departments] and two had the procedure after they were admitted for an exacerbation of their respiratory symptoms. Forty-five (72.5%) had wet/productive cough, thirty-eight (61.3%) recurrent pneumonia, fifteen (24.2%) atelectasis and thirteen (21%) bronchiectasis. Twenty-nine (47%) had both chronic wet/productive cough and recurrent pneumonia. Duration of symptoms was 24 (4–60) months. A chest CT scan had been done in 32 (56%) showing abnormalities in 27 (84%): bronchiectasis 13 (48%), consolidation 7 (26%), bronchial stenosis 3 (11%) and other (cavitation, granuloma, tracheal deformity, or bilateral interstitial pattern) in 4 (14.8%).

Forty-two (67.7%) had airways abnormalities at FB: malacia 32 (51.6%) [tracheomalacia 12 (19.4%), tracheobronchomalacia 11 (17.7%), bronchomalacia 9 (14.5%)], bronchial stenosis 12 (19%) 4 of them with associated bronchomalacia, and other abnormalities 5 (8%)