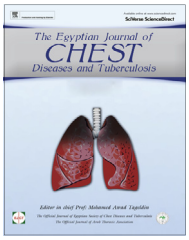
Egyptian Journal of Chest Diseases and Tuberculosis (2012) **61**, 243–246

The Egyptian Society of Chest Diseases and Tuberculosis

Egyptian Journal of Chest Diseases and Tuberculosis

www.elsevier.com/locate/ejcdt
www.sciencedirect.com



ORIGINAL ARTICLE

Effect of *Aspergillus Fumigatus* sensitization and colonization on lung function and airways inflammation in asthma

Ahmed E. Mansour [a,*], **Mohamed E. El-Desouky** [a], **Zeinab Beder** [b]

[a] *Department of Thoracic Medicine, Mansoura University, Egypt*
[b] *Department of Microbiology, Mansoura University, Egypt*

Received 10 September 2012; accepted 22 September 2012
Available online 24 January 2013

KEYWORDS

Asthma;
Lung function;
Aspergillus fumigatus;
Sputum neutrophil

Abstract *Background:* The sensitization and exposure to fungal allergens have been reported to be associated with asthma. The importance of *Aspergillus fumigatus* (AF) sensitization and colonization of the airways in patients with asthma is unclear.

Objectives: To clarify the effect of sensitization and airways colonization of AF on lung function and airways inflammation in asthma.

Methods: We studied 66 patients with asthma. Patients were classified into two groups according to AF sensitization: (1) AF-sensitized (immediate cutaneous reactivity >3 mm); and (2) AF-nonsensitized. A positive sputum culture for AF confirmed airways colonization by AF. Routine spirometry was performed for all patients. Airways inflammation was assessed by sputum differential inflammatory cell count.

Results: Asthma duration was significantly longer in AF-sensitized asthmatics. Significantly higher rates of positive AF-culture were detected in sputum from AF-sensitized asthmatics (63%) in comparison to AF-nonsensitized asthmatics (31%). FEV_1 and FEV_1/FVC were more reduced in AF-sensitized asthmatics in comparison to AF-nonsensitized asthmatics. Sputum neutrophils count was significantly higher in AF-sensitized asthmatics in comparison to AF-nonsensitized asthmatics. Sputum eosinophils did not differ between AF-sensitized and AF-nonsensitized asthma groups, concordant with peripheral blood eosinophils, which did not differ significantly between groups. Multilinear regression analysis predicting FEV_1 % showed that AF sensitization and sputum neutrophil count were the most important predictors of FEV_1 ($p = 0.016$ for both), followed by positive sputum culture for AF and sputum eosinophil count ($p = 0.024$ and 0.046 respectively). ($p = 0.105$).

* Corresponding author. Address: Department of Chest Diseases, Faculty of Medicine, Mansoura University, Mansoura 35516, Egypt.
E-mail address: amansour65@hotmail.com (A.E. Mansour).

Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

ELSEVIER **Production and hosting by Elsevier**

 http://dx.doi.org/10.1016/j.ejcdt.2012.09.006

Conclusions: AF detection in sputum is associated with AF-sensitization, neutrophilic airway inflammation, and reduced lung function. This supports the concept that development of fixed airflow obstruction in asthma is consequent upon the damaging effects of airway colonization with AF.

Introduction

The sensitization and exposure to fungal allergens such as *Aspergillus*, *Alternaria*, *Penicillium*, *Cladosporium*, and *Trichophyton* have been reported to be associated with asthma exacerbations and severity [1], and the frequency of exacerbations, treatment requirements, and admission to intensive care for asthma has been found to be associated with skin-test reactivity to one or more fungi [2].

Aspergillus spp. is ubiquitous within the indoor and outdoor environment, particularly in soil, decaying vegetation, and water-damaged building materials [3]. Inhalation of *Aspergillus* fumigatus (AF) spores can lead to airways colonization, recurrent airway inflammation, bronchial obstruction, mucoid impaction and proximal bronchiectasis with the development of allergic bronchopulmonary aspergillosis (ABPA) [4]. Allergic bronchopulmonary aspergillosis is the commonest form of allergic bronchopulmonary mycosis [5]. The term severe asthma associated with fungal sensitization (SAFS) was used to illustrate the high rate of fungal sensitivity in patients with persistent severe asthma (after exclusion of ABPA) and improvement with antifungal treatment [5]. However, the immunopathology of ABPA and SAFS is incompletely understood. Therefore; the aim of this study was to clarify the impact of sensitization and colonization of *Aspergillus* on lung functions and airways inflammation in asthmatics after exclusion of ABPA.

Methods

Subjects

Patients with stable asthma who had not been treated with maintenance oral corticosteroids were recruited. Inclusion required at least 12% improvement in FEV_1 15 min after 200 μg inhaled salbutamol. Exclusion criteria included respiratory disorders other than asthma, radiological evidence of bronchiectasis, smoking and comorbidities.

Spirometry

Spirometry was performed using a computed spirometer (Jaeger, Germany). Spirometry was performed three times and the best effort of FEV_1 was recorded. Reversibility was measured as change in FEV_1 15 min after 200 μg inhaled salbutamol.

Radiological examination

High-resolution computed tomography of the chest was performed. Crosssectional images were obtained using settings of 1-mm collimation at 10-mm intervals in full inspiration. Bronchiectasis was deemed to be present if there was bronchial dilatation (internal bronchial diameter greater than the accompanying pulmonary artery).

Skin prick test

Sensitization to AF was assessed using skin prick test (SPT). The development of a wheal > 3 mm in diameter indicates a positive test. SPTs and specific serum IgE tests are used to determine sensitization to various fungi [6]. We assessed "sensitization" solely on the basis of SPT results which were reported to be more sensitive than serum specific IgE tests to diagnose allergic sensitization in subjects with asthma or rhinitis [7].

Sputum examination

Sputum plugs were separated from saliva and divided into two parts. The first part was used for cytospins for a differential inflammatory cell count [8]. The second part was used for mycological culture. Undiluted sputum plugs were digested in equal volumes of 0.1% dithiothreitol then inoculated on Sabouraud agar containing 16 mg/ml chloramphenicol, 4 mg/ml gentamicin, and 5 mg/ml fluconazole. All plates were incubated at 37 °C and inspected frequently for up to 7 days. Subcultures of filamentous fungi were produced and AF colonies identified based on criteria for macroscopic morphology of colonies [9].

Statistical analysis

Data were analyzed with the Statistical Package for Social Sciences (SPSS, Chicago, IL). Quantitative data were presented in the form of mean ± standard error of mean. Qualitative data were presented in the form of numbers and percentages. Chi-square test was used to test differences of qualitative data. The quantitative data were tested by using *student's t-test*. A multilinear regression model was performed using the enter method for prediction of FEV_1%. A p value <0.05 was considered significant.

Results

Aspergillus fumigatus *sensitization*

According to the results of the cutaneous reactivity to AF, patients were divided into two groups: (i) AF-sensitized asthma (positive SPT) (ii) AF-nonsensitized asthma (negative SPT). The numbers of patients recruited to each group and their clinical characteristics are shown in Table 1. There were no significant differences in sex and age between groups. However; asthma duration was significantly longer in AF-sensitized asthmatics.