Egyptian Journal of Chest Diseases and Tuberculosis (2016) 65, 7–14

HOSTED BY

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

Association between anti-thyroid peroxidase and anti-cytokeratin 18 autoantibodies and bronchial asthma in women

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Received 12 August 2015; accepted 31 August 2015
Available online 26 September 2015

KEYWORDS

Allergic and non-allergic asthma;
Anti-TPO autoantibodies;
Anti-CK18 autoantibodies;
Thyroid function;
Total IgE

Abstract *Background:* The mechanisms of intrinsic or non-allergic asthma remain uncertain as allergens have no obvious role in driving the inflammatory process in the airways. This study was designed to test the possible presence of an autoimmune pathogenesis of bronchial asthma and to investigate the similarities and differences between allergic and non-allergic asthma.

Design: Cross-sectional prospective cohort study.

Subjects and methods: 50 asthmatic women and 30 healthy control women were tested for thyroid function, anti-TPO, anti-CK18 autoantibodies, and total IgE measurements. Pulmonary function tests, skin-prick test and history of asthma risk factors were done for asthmatic women.

Results: Allergic asthma were found in half of the asthmatic patients and the other half (25/50) were non-allergic according to the results of skin-brick test and serum level of IgE. The thyroid function tests were not statistically different between asthmatic and control groups as well as between non-allergic and allergic asthma groups ($P > 0.05$). Serum anti-TPO autoantibodies and anti-CK18 autoantibodies' levels were significantly higher in asthmatic patients than the control group and also in non-allergic asthma patients than allergic asthma patients. In asthmatic patients serum anti-TPO autoantibodies showed negative correlation with FEV1 (pre- and post) and serum IgE.

Conclusion: Positive anti-TPO autoantibodies and anti-CK18 autoantibodies in asthmatic patients and their higher level in the non-allergic asthma group may strengthen the presence of a hidden autoimmune phenomenon in non-allergic asthma.

Abbreviations anti-TPO autoantibodies, anti-thyroid peroxidase antibodies; anti-CK18 autoantibodies, autoantibodies to cytokeratin 18; IgE, immunoglobulin E; Hb, hemoglobin; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; FEF, forced expiratory flow; CBC, complete blood picture; COPD, chronic obstructive pulmonary disease

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

http://dx.doi.org/10.1016/j.ejcdt.2015.08.018

Introduction

Bronchial asthma is as a heterogeneous disease, usually characterized by chronic airways inflammation. It is defined by the history of respiratory symptoms such as wheezes, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation [1].

Asthma is a problem worldwide with an estimated 300 million affected individuals [2]. The global prevalence of asthma range from 1% to 18% of the population in different countries [3,4]. In Egypt, the bronchial asthma is a significant health problem among school children, and the prevalence was 7.7% [5]. Annual world deaths from asthma have been estimated at 250,000. Asthma is a major cause of absence from work in many countries [6–8].

Malfunction of the immune system is known in three main conditions: immunodeficiency, allergy, and autoimmunity. The appearance of autoimmunity and allergies has not been well appreciated. Recently, there are reports on the appearance of allergies concomitantly with autoimmunity, but the relationship is poorly understood. Allergy and autoimmunity are two potential outcomes of dysregulated immunity. Both are characterized by localized inflammation that leads to the injury and/or destruction of target tissues [9]. The allergic response to common environmental agents (allergens) has been regarded as an important mechanism in the development of airway inflammation of patients with asthma. However, allergic sensitization cannot be detected in a significant number of adult patients with asthma [10]. Non-allergic asthma usually begins at an older age and is clinically more severe than allergic asthma. Non-allergic asthma has been referred to as "intrinsic asthma" on the basis of a belief that there must be an etiologic agent in the patient's own body. However, the "intrinsic" etiology has not yet been defined [11].

One of the most important causes of thyroid diseases is autoimmunity in origin, and it seems that people with thyroid diseases present more signs of asthma. A little is known about the relation between thyroid disease and allergic diseases. The pathogenic mechanism for relationship between thyroid dysfunction and severity of asthma signs is not clearly understood. Knowledge of the presence of thyroid disease in patients with bronchial asthma is important. The reason is that hypothyroidism may coexist with allergic diseases such as bronchial asthma, while hyperthyroidism may be associated with a lower incidence of allergies. Some studies have shown that hypothyroidism ameliorates and hyperthyroidism exacerbates bronchial asthma [12].

The idea of the possible involvement of an autoimmune mechanism in the pathogenesis of asthma has been proposed by previous studies that demonstrated high incidences of circulating autoantibodies to bronchial mucosa tissue (as anti-CK18 autoantibodies) in patients with asthma, especially in patients with non-allergic asthma [13–15].

This study was designed to investigate the frequency of autoimmune phenomena with and without thyroid diseases in women suffering from bronchial asthma by measuring serum level anti-TPO autoantibodies and anti-CK18 autoantibodies.

Subjects and methods

This study was conducted on 80 women over 18 years. Fifty of them had bronchial asthma whatever severity and thirty of them were healthy non-asthmatic. Women who attended to outpatient clinic at chest department and internal medicine department of El-Minia University Hospital were invited to participate in the study. The study was approved by the hospital's research ethics board.

Exclusion criteria

Women who had the diagnosis of COPD, connective tissue diseases, congestive heart failure, chronic renal failure or positive history of definite thyroid diseases or being under treatment were excluded. Pregnant and smoking women were also excluded.

The control group consisted of 30 women selected from people who participated in a field trial study. This group had no symptoms or signs of asthma disease in addition to all the above exclusion criteria.

The asthmatic patients were selected based on having characteristic respiratory symptoms such as wheezing, dyspnea, chest tightness or coughing and variable expiratory airflow limitation. Variable expiratory airflow limitation was confirmed by spirometry (ZAN 300, Germany). Reversibility refers to rapid improvement in FEV1 (12% and 200 ml) measured within minutes after inhalation of 400 μg of salbutamol [16]. Asthma severity was graded based on guidelines for diagnosis and treatment of asthma. Four groups; mild intermittent, mild persistent, moderate persistent and severe persistent were considered [17].

All asthmatic subjects underwent a skin-prick test with 12 common aeroallergens based on common aeroallergens in our region: mites, molds, pollens, animal dander, pigeon, house dust, feather, cats, strew and Candida. Histamine and saline were used as positive and negative controls. Patients with asthma were classified as having allergic asthma when the wheal diameter of any one allergen was greater than 3 mm over the negative control (normal saline) and there was a definite clinical history or objective evidence of asthmatic response induced by allergen exposure. Non-allergic asthma was defined as there being no positive skin reaction to any of the 12 common aeroallergens in the presence of a positive histamine control and serum total IgE concentration being within the normal range (less than 180 IU/ml). All patients with asthma had not received systemic steroid treatment for the 4 weeks before the study.

Five ml of venous blood was taken by sterile venipuncture after informed consent of all participants and divided as follows: one ml on EDTA for CBC, 4 ml on plasma tube was left to be collected and centrifuged to separate serum, and then serum was freezed at −70 °C for assay of anti-CK18 autoantibodies, total IgE, Anti-TPO, total T4 and TSH. All were measured by the EIA (Enzyme immune-assay) method using Huma reader, Germany.

Kits of Anti-TPO autoantibodies were supplied by Bios, USA, chemux Bioscience. Kits of autoantibodies to anti-CK autoantibodies were supplied by orgentec, diagnostic, Germany. Kits of total IgE were supplied by orgentec, diagnostic,