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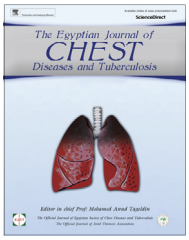

ORIGINAL ARTICLE

Role of autoimmunity in the pathogenesis of chronic obstructive pulmonary disease

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KEYWORDS

COPD;
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Abstract *Background:* Chronic obstructive pulmonary disease (COPD) is a major factor for disease related loss of quality of life, health expenditure and loss of productivity. An enhanced and persistent inflammatory response to the inhalation of particles and gases, mostly tobacco smoking, is considered a key pathogenic mechanism of COPD. Recent evidence indicates that autoimmunity plays a significant role in this response.

Aim of the work: This study investigated the role of autoimmunity in the pathogenesis of COPD by determining the prevalence of circulating autoantibodies in these patients and in healthy controls and evaluating their relationship with several disease components.

Patient and methods: This study included 31 COPD patients and 12 healthy non-smoker controls. All individuals were subjected to detailed history taking, full clinical examination, BMI calculation, arterial blood gas analysis, spirometry, 6MWD and assessment of serum level of circulating autoantibodies.

Abbreviations: COPD, chronic obstructive pulmonary disease; BMI, body mass index; 6MWD, 6 min walk distance; ABG, arterial blood gases; PaO_2, partial pressure of arterial oxygen; $PaCO_2$, partial pressure of arterial carbon dioxide; SaO_2, oxyhemoglobin saturation; CD4+, cluster of differentiation helper T lymphocytes; CD8+, cluster of differentiation cytotoxic T lymphocytes; BALT, bronchus associated lymphoid tissue; FVC, forced vital capacity; FEV1, forced expiratory volume in 1st second; ATS, American Thoracic Society; ANA, antinuclear antibodies; Ds-DNA, double stranded DNA; AT, anti-tissue autoantibodies; AMA, anti mitochondrial autoantibodies; SMA, smooth muscle autoantibodies; PGC, parietal gastric cell; IFI, indirect immunofluorescence; SD, standard deviation; *P*-value, probability value; SPSS, statistical package for the social science; SLE, systemic lupus erythematosus; α1-antitrypsin, alpha 1-antitrypsin; IgG, Immunoglobulin G; RA, rheumatoid arthritis; TNF-α, tumor necrosis factor alpha; IL-6, interleukin-6; IL-8, interleukin-8; CPFE, combined pulmonary fibrosis and emphysema syndrome; IPF, idiopathic pulmonary fibrosis; P-ANCA, perinuclear anti-neutrophil cytoplasmic antibodies; CD20, cluster of differentiation antigen 20; DLCO, diffusing capacity for carbon monoxide; ENA, extractable nuclear antigen; GOLD, global initiative for chronic obstructive lung disease; AARC, American Association for Respiratory Care

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Results: There was a statistically significant difference between COPD patients and healthy controls in the spirometric data, PaO_2, SO_2 and 6MWD; however there was no statistically significant difference between both groups in the prevalence of autoantibodies. Also there was no statistically significant correlation between the prevalence of autoantibodies and other variables such as age, BMI, 6MWD, spirometric and ABG parameters.

Conclusion: The prevalence of positive circulating autoantibodies in COPD patients was found not significant when compared with healthy non smoker control group. This finding does not support a role for autoimmunity in the pathogenesis of COPD. So the hypothesis that autoimmunity plays a role in the pathogenesis in COPD needs further exploration.

Introduction

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients [1].

It is now increasingly recognized that (COPD)/emphysema presents clinically as a syndrome with pulmonary and extrapulmonary manifestations [2]. Interestingly, only 15–20% of smokers develop COPD, suggesting that genetic predisposition and environmental factors play a role in the pathogenesis of the disease [3].

It has been hypothesized that there may be an autoimmune component to the chronic progressive lung tissue destruction which can persist after smoking cessation [4,5].

There is some evidence to support the contention that there is increased acquired immunity in COPD: (1) both helper (CD4+) and cytotoxic T lymphocytes (CD8+) accumulate in the lung parenchyma of patients with COPD [6]; (2) B lymphocytes form the core of the so-called bronchus-associated lymphoid tissue (BALT) which has been shown to be significantly increased in smokers and in patients with COPD [7,8]; (3) smoking is associated with an expansion of the population of antigen presenting cells on the epithelial surface of the lower respiratory tract [9].

The aim of the present study was to explore the role of autoimmunity in the pathogenesis of COPD by determining the prevalence of circulating autoantibodies in patients with COPD and healthy controls and evaluating their relationship with age, body mass index, spirometric parameters and arterial blood gases.

Subjects

The present study included thirty one male patients who fulfilled the criteria for COPD according to the American Thoracic Society/European Respiratory Society recommendations [10]. All patients were $\geqslant 50$ years of age and $\geqslant 10$ pack-year history of cigarette smoking. They were stable at the time of the examination with no other comorbid conditions or autoimmune diseases. Also patients younger than 45 years of age and patients with other pulmonary lesions e.g.; cancer, residual extensive tuberculous lesion or pulmonary fibrosis were excluded.

The control group included twelve healthy male controls with no smoking history.

Methods

All included individuals were subjected to: detailed history taking, full clinical examination, plain chest X-ray (P–A view) to exclude other chest problems. Body mass index, flow/volume loop using body plethysmography with highly transparent box; Sensor-medics V max series, 2130 Spirometer, V6200Autobox, 6200DL, arterial blood gases to estimate $PaCO_2$, PaO_2 and SO_2 using a blood gas analyzer (PHOX PLUS C), six min walk test and serum level of circulating autoantibodies.

Body mass index (BMI), or quetelet index

It is defined as the individual's body weight divided by the square of their height with the value universally being given in units of kg/m^2 [11].

Pulmonary function test

(Flow/volume loop): spirometry indices are reported comparing the individual's value along with the predicted values. The forced vital capacity (FVC), the forced expiratory volume in the first second (FEV1), the ratio of FEV1 to FVC and the forced expiratory flow at 25–75% of FVC (FEF25–75%) were measured. The presence of a post bronchodilator FEV1/FVC ratio <0.70 confirms the presence of airflow limitation. Bronchodilator challenge test was performed to confirm that the air flow limitation is not fully reversible. Reversible airway obstruction is considered significant when there is an increase in the pre-bronchodilator FEV1 by both greater than 200 ml (*absolute change*) and 12% (% *change*) [12].

Arterial blood gases

One ml of arterial blood was obtained from the radial artery in a heparinized syringe, once the sample is obtained, care is taken to eliminate visible gas bubbles, as these bubbles can dissolve into the sample and cause inaccurate results. The sealed syringe is taken immediately to a blood gas analyzer (PHOX PLUS C) which aspirates this blood from the syringe and measures the partial pressures of arterial oxygen, carbon dioxide and oxygen saturation [13].