EFFECT ON LUNG STRUCTURE, INFLAMMATORY AND NUTRITIONAL STATUS OF COPD PATIENTS WITH FIBROTIC AND PROLIFERATIVE TUBERCULOSIS CHANGES IN CHEST IMAGING

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Abstract

Background and objectives Tuberculosis and COPD are common diseases in developing countries, sharing risk factors like smoking and low socio-economic status but little is known about the specific relationship between tuberculosis and COPD.

Methods Retrospective analysis was done. All COPD patients with either fibrotic and proliferative tubercular changes in chest imaging or none of the features of tuberculosis (in chest imaging, sputum test, skin test or history) admitted in Sun Yat- Sen Memorial Hospital, China from the year 2007 to 2010 were taken for the study. Clinical features along with post–bronchodilator FEV1/FVC<70% were used as a basis for the diagnosis of COPD.

Results Among 84 COPD patients with fibrotic and proliferative tuberculosis changes in chest imaging, 20 of them had bullae or blebs in their radiologic examination whereas only 11 of 105 non-tuberculosis COPD cases had those features, Pearson Chi Square value=6.05, p=0.014. COPD patients with fibrotic and proliferative tuberculosis changes had lower blood iron, transferrin, albumin but higher high sensitive CRP (hsCRP) (p=0.010, 0.003, 0.010 and 0.032 respectively) compared to non-tuberculosis COPD cases.

Conclusions Fibrotic and proliferative tuberculosis changes in COPD results in greater inflammation and damage to lung tissue (determined by increase bullae formation, higher hsCRP level) with decrease in basic nutritional elements.

Key words: *Biochemistry, COPD, Inflammation, Lung injury, Tuberculosis*

Introduction

COPD and tuberculosis mainly affect lungs and are major causes of morbidity and mortality worldwide. Around a third of world population is infected with tuberculosis, with about eight million new cases being reported every year [1]. Prevalence of COPD is increasing. It is estimated that COPD will become the third-leading cause of death by 2020 [2]. Both COPD and tuberculosis have common risk factors such as smoking and low socio-economic status [2, 3]. So, it is necessary to know the relationship between tuberculosis and COPD.

This study was conducted in a hospital of southern China where tuberculosis and COPD are among the most common diseases seen in respiratory department. Aims of this study were to investigate any structural changes in lungs as well as to assess any inflammatory and nutritional changes in COPD patients with fibrotic and proliferative

tuberculosis changes in chest imaging compared to non-tuberculosis COPD cases.

Methodology

Patient Selection and Data collection: This was a retrospective study approved by our hospital's institutional review board. All the COPD patients either with fibrotic and proliferative tuberculosis changes in chest imaging or none of the features of tuberculosis (in imaging, sputum test, skin test or history) from the year 2007 to 2010 were taken for the study. Diagnosis of COPD was confirmed by the clinical features and post-bronchodilator FEV_1/FVC less than 70%. These patients were admitted in respiratory department due to acute exacerbation of COPD. Among these 189 COPD patients; 84 of them had fibrotic and proliferative tubercular changes in chest imaging with negative tubercular sputum smear test and PPD value less than 10mm whereas rest 105 of them had all these three tests negative.

There was no statistical difference in age and pack year between COPD patients with fibrotic and proliferative tuberculosis changes compared to non-tuberculosis COPD cases. Average age of COPD patients with tubercular changes was 75(69-79) years old compared to 72(67-77) years old in non-tuberculosis COPD cases, p=0.076. Average smoking pack-years in tuberculosis group was 40(30-50) compared to 40 (20-60) in non-tuberculosis group, p=0.537. There was also no statistical difference in gender in between the two groups, Pearson Chi-square value being 3.188, p=0.074 (as shown in table 1).

Table 1. Baseline parameters of the COPD patients in our study

Parameters	Tuberculosis	Non-tuberculosis	p value
Number	84	105	
Gender(male: female)	72:12	79:26	0.149
Age	75(69-79)years	72(67-77)years	0.076
Smoking	40(30-50)pack-year	40(20-60)pack-year	0.537

Exclusion Criteria: COPD patients with active tuberculosis, occupational lung diseases, asthma, any part of the documented cancer, liver and kidney diseases were all excluded in this study.

Statistics: SPSS 16 was used for the analysis. Normality test was done and normal cases were analyzed with independent sample t-test whereas Mann-Whitney test was done for those not following normal distribution. Chi-square test was used for qualitative data. A p value of <0.05 was considered to be statistically significant.

Results

Comparison of bullae or blebs formation in COPD patients with proliferative tuberculosis changes compared to non-tuberculosis COPD cases. Out of 84 COPD patients with fibrotic and proliferative tuberculosis changes in chest imaging, 20 (23.8%) of them had significant bullae or blebs in their chest images. But in case of 105 non-tuberculosis COPD cases, obvious bullae were seen only on 11 patients (10.5%) in their chest imaging. Chi Square test was done to compare the incidence of bullae in two groups and it was found that COPD patients with fibrotic and proliferative tuberculosis changes in chest imaging had higher incidence of bullae or blebs compared to non-tuberculosis COPD cases, with Pearson Chi Square value of 6.05, p=0.014.

Comparing inflammatory and nutritional status in COPD patients with fibrotic and proliferative tuberculosis changes compared to non-tuberculosis COPD case. While investigating the difference in Hb, high sensitive CRP (hsCRP), calcium, albumin, iron, transferrin between COPD patients with

fibrotic and proliferative tuberculosis changes and non-tuberculosis COPD cases, we first did normality test. Those following normal distribution were done independent sample t-test to find out the difference, and the result showed statistical difference in blood albumin (37.7±3.6 g/L vs. 39.0±3.1 g/L, p=0.010) and transferrin (1.82±0.36 g/L vs. 1.97±0.34 g/L, p=0.003) in tuberculosis group compared to non-tuberculosis COPD patients. Mann-Whitney non-parametric test was done for those not following normal distribution. Result showed statistical difference in hsCRP {21.1(4.9-80.5) mg/L vs. 10.3(2.3-44.3) mg/L, p=0.032}, blood iron {8.8(5.6- 17.3) µmol/L vs. 12.2 (8.0-17.3) µmol/L, p=0.010} in COPD patients with fibrotic and proliferative tuberculosis changes in chest imaging compared to non-tuberculosis COPD cases (shown in table 2).

Table 2: Inflammatory and nutritional markers in two different COPD groups

Parameters	Non Tuberculosis	Tuberculosis	p value
hsCRP *	10.3(2.3-44.3)mg/L	21.1(4.9-80.5)mg/L	0.032
Iron	12.2(8.0-17.3)µmol/L	8.8(5.6-17.3) µmol/L	0.010
Albumin	39.0±3.1g/L	37.7±3.6g/L	0.010
Calcium	2.22(2.10-2.30)mmol/L	2.20(2.07-2.30)mmol/L	0.227
Hb	133(122-140)g/L	132(122-141)g/L	0.949
Transferrin	1.97± 0.34 g/L	1.82± 0.36 g/L	0.003

*hsCRP: high sensitive CRP

Discussion

Structural changes of lung in COPD patients with fibrotic and proliferative tuberculosis changes compared to non-tuberculosis COPD patients**.**

In this study, there was higher incidence of bullae or blebs in COPD patients with fibrotic and proliferative tuberculosis changes in chest imaging compared to non-tuberculosis COPD individuals, Pearson Chi square value 6.05, p=0.014.Tuberculosis can increase the activity of matrix metalloproteinase (MMP) enzymes, similar to that done by smoke exposure, thereby damaging the lung tissue [4]. Increase in activity of MMP enzymes results in destruction of collagen and other internal structures of lung parenchyma. This may result in increased formation of bullae in these groups. Tuberculosis results in scarring of lung tissue and thereby pulls the normal lung tissue towards affected part. This can be the pathological mechanism for increase in bullae formation in tuberculosis infected COPD patients.

Inflammation and nutritional derangement in COPD patients with pulmonary tuberculosis**.**

To best of our knowledge, this is the first study evaluating inflammation and nutritional status in COPD patients with fibrotic and proliferative tuberculosis changes in chest imaging compared to non-tuberculosis COPD cases. It was found that COPD patients with pulmonary tuberculosis infection had higher hsCRP but lower blood iron, albumin, and transferrin compared to COPD patients without tuberculosis.

CRP is an acute phase protein produced by liver under the influence of IL in response to injury or tissue damage. A high sensitivity CRP (hsCRP) measures even low level of CRP. Circulating CRP levels are elevated in blood of stable COPD patients [5]. CRP is also used to predict the prognosis in terms of hazard ratios for hospitalization and death from COPD [6]. In this study, higher hsCRP value in COPD patients with fibrotic and proliferative tubercular changes in chest imaging than COPD patients without pulmonary tuberculosis suggests that there can be greater damage to lung and can have more severe form of COPD leading to poorer prognosis in the former subtype.

In this study, it was found that COPD patients with fibrotic and proliferative tubercular changes in chest imaging had lower blood iron and transferrin value

compared to COPD patients without tuberculosis. This can be the scenario of chronic illness. Ratledge had described the role of iron in the pathogenesis of tuberculosis [7]. Host tries to limit infection by lowering iron. But pathogens adapt by increasing the expression of virulence factors and cause damage to the host. Administration of iron in this condition is unfavourable, as increased availability of iron can help the bacteria to multiply. Lower blood iron in COPD patients with proliferative tuberculosis changes can have some protective role in preventing the conversion of this old tuberculosis into active form or it can be due to metabolism of iron in chronic disease. Large scale study is needed to confirm the role of iron in tuberculosis infected COPD patients.

Levels of transferrin decreases in inflammation [8] and is referred as a negative acute phase reactant. Although transferrin is the principal iron binding protein in serum, it is also present in airway mucosa and alveolar lining fluids [9]. Transferrin functions as an antioxidant by tightly binding extracellular iron and thereby inhibiting oxidant induced lipid peroxidation both in serum and lower respiratory tract [10, 11]. It may also have important antibacterial effects in lower respiratory tract by sequestering iron that is needed for bacterial multiplication [12]. Decrease in transferrin level in COPD patients with fibrotic and proliferative tuberculosis changes compared to non-tuberculosis COPD cases can therefore point out that there is greater inflammation ongoing in these former patients.

Some studies had shown that there is reduced serum albumin in patient with active tuberculosis [13-15]. Little is known about albumin level in patients with radiologic features of old pulmonary tuberculosis. Ugur et al reported that serum albumin decreased with decline in lung function [16]. Like transferrin, albumin level decreases during inflammation and is also referred as negative acute phase reactant [8]. In this study, it is found that COPD patients with fibrotic and proliferative tuberculosis changes in their chest imaging had lower blood albumin value compared to COPD patients without tuberculosis. This finding may be due to greater damage in lung leading to more severe inflammation in tuberculosis infected group.

COPD phenotype is a hot topic in recent literatures. It is considered that COPD patient with fibrotic and proliferative tuberculosis changes in chest imaging should be recognized as a new phenotype and should be treated with great caution, as the use of inhaled corticosteroid (as an anti-inflammatory treatment) in this subtype carries certain risk of conversion of old tuberculosis into active form. Whether to treat COPD patient with fibrotic and proliferative tuberculosis changes in chest imaging with anti-tuberculosis therapy is also of great concern, making this phenotype to be given greater emphasis in coming days.

In conclusion, COPD patients with fibrotic and proliferative tuberculosis changes in chest imaging had greater inflammation and damage to lung tissue (determined by increase bullae formation, higher hsCRP level) with decrease in basic nutritional elements compared to non-tuberculosis COPD cases.

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