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PRESENCE OF ATOPY IN BRONCHIECTATIC PATIENTS: A NOT SO COINCIDENTAL FINDING.

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ABSTRACT

Bronchiectasis, a common clinico-radiological finding in developing countries, turns out to be idiopathic in around 45% cases.[1,2] Previous studies trying to establish a correlation between frequency of Atopy and radiological and lung function findings in bronchiectasis, are limited in number with results being controversial.[3] This study was designed to enquire into the relationship between atopy and bronchiectasis using High resolution CT (HRCT) scans and spirometry. Skin prick test, HRCT and spirometry, including values of forced expiratory volume in one second (FEV1), FEV1/FVC (Forced Vital Capacity) ratio were performed in 130 patients of bronchiectasis of unknown etiology and in 70 healthy controls. Atopy and HRCT scores for the severity of Atopy and extent of bronchiectasis respectively were determined for each patient. The rate of Atopy (46.2% vs 12.9%) and mean atopy score (13.2 +- 10 mm vs 5.3 +- 2mm) were significantly higher in bronchiectatic patients than in controls. The extent of bronchiectasis, with worse spirometric values were observed in atopics than non atopics. We also observe that there is a significant correlation between atopy and HRCT score ($r = 0.56$; $p<0.001$), indicating that severe the atopy, worse is the bronchiectasis. In conclusion, we propose that the rate of atopy is higher in patients with bronchiectasis than in healthy controls. Also, bronchiectatic patients with atopy have lower spirometric values and higher HRCT scores. Atopy thus can be considered as a contributing and a detrimental factor for development of bronchiectasis.

INTRODUCTION

Bronchiectasis is defined as permanent, abnormal dilatation of the bronchial tree. Bronchiectasis, quite common in developing countries, is not a disease per se, but an end stage manifestation of a variety of pathologic processes seen in various diseases. 40% of cases of bronchiectasis have a precise underlying mechanism, with 15% patients developing from specific treatment.3,4 HRCT, besides being the diagnostic tool of choice, contributes to clinical management of the disease.

Although an increased prevalence of reversible airway obstruction, bronchial hyperreactivity, atopic diseases such as asthma have been reported in patients with bronchiectasis (Varpela et al.1978; Murphy et.al. 1984; Pang.et.al. 1989; Ip et al. 1991, 1992; Hasan et al. 1999), the results of the studies in the literature investigating the frequency of atopy in bronchiectasis are a few in number and controversial.[5,6] Moreover, there are no data in the literature about the relation of atopy with lung function and radiologic extent on HRCT in patients with bronchiectasis.

In view of this conflicting data, we aimed to investigate prospectively the frequency of atopy to inhaled allergens and its relationship to the extent and severity of the disease on HRCT and pulmonary function in patients with bronchiectasis.

METHODS AND MATERIALS

Subjects: The study was conducted at Department of Pulmonary Medicine, Patna Medical College and Hospital, Patna, Bihar, India, which is a teaching hospital. From March 1, 2020 to December 31, 2022, all consecutive patients with bronchiectasis admitted to our department were enrolled to the study. Patients with any known cause of bronchiectasis including cystic fibrosis, established diagnosis of bronchial asthma and Allergic Broncho Pulmonary Aspergillosis, previous tuberculosis, humoral immunodeficiency, autoimmune and collagen vascular diseases and α1 antitrypsin deficiency were excluded. Finally, 130 patients with bronchiectasis without any known etiology were included. Patients characteristics including age, sex, smoking history, disease duration, history of familial atopy, childhood and current allergic diseases were recorded. Since bronchial asthma were excluded from the inclusion criteria, current allergic diseases included atopic dermatitis and allergic rhinitis. Seventy healthy subjects who are free of any allergic disease such as asthma and allergic rhinitis serve as controls. An informed consent was obtained from all study subjects and the study was approved by the local ethics committee of PMCH.

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Diagnostic criteria and HRCT scoring

In all patients, HRCT scans with 1mm collimation at 10mm intervals were obtained through the thorax at end inspiration and they were interpreted by two radiologists who were blinded to clinical history and chest x ray findings. Criteria for the diagnosis of bronchiectasis utilizing HRCT included the following: 1) dilatation of the bronchi as determined by increased bronchial/adjacent pulmonary artery ratio (ratio>1) when imaged in cross section (signet-ring sign), 2) Parallel bronchial walls when seen in cross section (tram sign), and 3) demonstration of bronchi at peripheral third of the lung (Pifferi et al. 2004). Bronchiectasis was scored as previously described (Twiss et al. 2005) using the modified Bhalla scoring system (Bhalla et al. 1991; Roberts et al. 2000).[7] The score has been validated in adult and pediatric patients with bronchiectasis and assigns a value to each lobe and the lingula as follows: Bronchiectasis extent (0-3), bronchial wall dilatation (0-3) and thickness (0-3), presence of mucus in large airways (0-1) and small airways (0-1), air trapping (0-4), atelectasis (0-1) and consolidation (0-1) resulting in worst possible score of 102 (Roberts et al. 2000). The highest HRCT score represented the more extended and severe bronchiectasis.[8,9]

Spirometry

Lung function measurements were performed using a spirometer (Sensorimedcs 2400, Sensorimedics company, Bilthoven, Netherlands) according to the standardized procedures of the European Respiratory Society. Volume calibration of the spirometer was done before each measurement. The Forced Vital Capacity (FVC) and the forced expiratory volume in 1 second (FEV1) were taken as the highest readings obtained from at least three satisfactory forced expiratory maneuvers. The participants' baseline lung function was compared with the reference value of Knudson et al. (1976) and expressed as percent of the predicted values.

Skin prick test

Skin Prick Tests (SPT) were performed by allergists at PMCH according to a routine procedure and using a standard panel of 56 common aeroallergens including mites (D. farinea and D. pteronyssimus), molds, grass mix, tree mix pollen, weed mix, cockroach and animal dander (Green Lab, NC, USA). Drugs that depress the immediate type skin tests such as antihistaminics or tricyclic antidepressants were discontinued 7 days prior to the test. SPT were applied on the volar surface of the forearm by the same investigator using disposable lancets and reactions were recorded 15 minutes after the test. Resulting wheal diameter larger than 3mm with surrounding erythema was considered as positive for atopy if the positive control histamine was positive and negative control was negative. To differentiate demographic and irritant reactions, test with negative control solution (diluent with 0.9% saline and 0.4% phenol) was particularly performed to all subjects. The wheal without erythema was accepted as irritant reaction and was excluded. An atopy score for the degree of atopy was calculated as the sum of mean wheal diameter of 56 allergens tested, as previously defined. (Koh et al. 2002).[10,11,12] The higher atopy score was considered as having the more severe atopy.

Statistical Analysis

SPSS (SPSS for Windows, SPSS Inc., Chicago, IL, USA) statistical package were used for statistical analysis. Descriptive statistics were shown as mean

Results

The patients were divided in two groups- atopic and non atopic and levels of significance were tested. There were more number of male patients in our study but the demographic characteristics and smoking habits of the groups did not show a significant difference. In 130 patients with bronchiectasis, whose mean age was 25.0 +-6.5 and of whom 110 were male, +- S.D. Univariate analysis was performed using the Chi-square test for proportion of atopy, sex differences in the study and control groups. To compare parametric values of the groups including age, disease duration, mean HRCT and atopy scores and lung function parameters, Student's t-test was used. Correlation of the atopy score with lung function parameters and HRCT score was investigated by Pearson correlation test. A p value less than 0.05 was considered statistically significant. 60 (46.2%) patients were assessed as atopic, while only 10 (12.9%) of the 70 controls were atopic ($p<0.001$). The most common allergen was house dust mites (40%). The frequencies of positive results with other allergens including grass pollen, tree pollen, weed pollen, cockroach and molds among patient with bronchiectasis were 13%, 8%, 8%, 8% and 6% respectively. When patients with bronchiectasis and the controls were compared according

to specific allergen sensitivity, patients with bronchiectasis had significantly more positive reactions to house dust mites and weed mix than controls ($p< 0.001$ and $p< 0.036$, respectively) while sensitivity to other allergens did not differ significantly between the groups. Mean atopy score (per atopic subject) was significantly higher in patients with bronchiectasis (13.2 +- 10 mm; $p< 0.001$) than in controls (5.3 +- 2mm). Study group had also significantly reduced pulmonary function with respect to controls. Mean HRCT score was significantly higher in atopic patients (33.5 +- 12) with bronchiectasis than in those non atopic (18.5 +- 8.5). Atopic patients also had significantly reduced FEV1 (62.5 +-10.5%; $p< 0.001$) and FEV1/FVC (66.0+- 7.5%) values, longer disease duration, frequent history of familial atopy, childhood and current allergic diseases than non atopics. Smoking habit did not differ significantly between atopics and non atopics. Atopy score was correlated positively with HRCT score ($r = 0.56$ and $p <0.001$) and negatively with FEV1 ($r = -0.5$ and $p <0.001$) values.

DISCUSSION

The study demonstrated that atopy is more frequent in patients with bronchiectasis than in healthy individuals. Atopic patients with bronchiectasis had significantly worse pulmonary function and higher HRCT score, which was indicated more extended and severe bronchiectasis than their non-atopic counterparts. Furthermore, atopic score was correlated positively with HRCT score and negatively with pulmonary function parameters of FEV1 and FEV/FVC. These findings indicate that the more severe atopy results in the worse pulmonary function and the more extended and severe bronchiectasis. House dust mites was the major allergen among bronchiectatic patients and atopic patients had longer disease duration than their counterparts.

Bronchiectasis is characterized by bronchial obstruction and hyper reactivity of which mechanisms are not well understood. It has been suggested that mucosal edema, glandular hyperplasia, excessive airway collapse in expiration might lead to bronchial obstruction. Association of atopy and allergic diseases such as asthma and alteration of bronchial smooth muscle and autonomic neural regulation due to increased access to toxins through infected or inflamed bronchial mucosa could cause bronchial hyperactivity. It has been suggested that coexistence of asthma with bronchiectasis alone cannot explain bronchial hyperreactivity and obstruction. According to our results, lower pulmonary function in atopic bronchiectatic patients than non atopics indicate that atopy may have a role in bronchial obstruction in bronchiectasis.

The previous studies yielding results different from ours have methodological differences.

The study of Varpela et al. (1978) was uncontrolled and diagnosis of bronchiectasis was based on bronchography, which is less sensitive than HRCT. SPT was carried out with only 11 allergens in the study of Pang et al. (1989). Although Murphy et al. (1978) reported that no increased prevalence of atopy in patients with bronchiectasis were observed compared to healthy controls, patients with positive SPT results showed a larger mean wheal diameter (mean atopy score) than controls with positive responses and they used bronchography to diagnose bronchiectasis, instead of HRCT. The study of Hasan et al. (1999) supports our diagnosis, but their study was uncontrolled.[13,14] Our study population was larger than those mentioned above and significant correlations of atopy score with HRCT score and lung function have been reported for the first time in literature. The method for atopy scoring needs to be validated and standardized in further studies. The male predominance is yet another limitation of our study, but we suppose these limitations do not invalidate our findings.

One may have thought that our results are conflicting with that of *hygiene hypothesis* with regard to development of atopy and allergic diseases, but we suppose that our study do not contradict the *hygiene hypothesis* and association of bronchiectasis and atopy can be explained from several points of view. Firstly, some infections that may be associated with both atopy and bronchiectasis such as measles, pertussis and staphylococcal infections might have taken part in the development of bronchiectasis at the same time, as does allergic bronchopulmonary aspergillosis.

Secondly, coincidence of bronchiectasis and some other infections such as Hepatitis B virus (HBV) infection that can potentially induce atopy may be another explanation of association of bronchiectasis and atopy.

Thirdly, different inflammatory responses to infections and high incidence of comorbidity with bacterial infections including sinusitis in atopic subjects may be a contributing factor in pathogenesis of bronchiectasis.

CONCLUSION

Thus, we suppose that atopy may be a contributing factor on development of bronchiectasis, as well as a coincidence, since the incidence of bronchiectasis can be higher than

expected in countries where atopy prevalence is also high. Moreover, atopy can be a detrimental factor for bronchiectasis since atopy score has been positively correlated with HRCT score. In other words, more the atopy, more extended is the bronchiectasis. Thus, clinicians must be aware of the proposition that atopy is significantly frequent in bronchiectasis, and it may worsen pulmonary functions and more radiologically extended bronchiectasis. However, it further needs to be investigated by epidemiological and immunological studies.

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