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Neutrophilic asthma has different radiographic features to COPD and smokers

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Summary
Background: Neutrophilic asthma and COPD are obstructive airway diseases common in older age and have a characteristic airway inflammation with neutrophilic bronchitis. The structural differences between neutrophilic asthma and COPD have not been investigated. The aim of this study was to examine the airway and parenchymal abnormalities using high resolution computed tomographic (HRCT) scanning in participants with neutrophilic asthma, COPD and smoking controls.
Methods: Participants (neutrophilic asthma ($n = 10$), COPD ($n = 17$) and smoking controls ($n = 8$)) underwent clinical assessment and sputum induction. HRCT of the chest was performed and independently scored by a radiologist blinded to the subject group using a modified Bhalla scoring system.
Results: Participants were of a similar age and those with COPD had a similar degree of airflow obstruction to those with neutrophilic asthma. The pattern of radiographic abnormalities differed between groups. Abnormal bronchial wall thickening was significantly more common in neutrophilic asthma, compared to COPD or smoking controls. Emphysema was greatest in the COPD group, and not recorded as a feature of neutrophilic asthma. FEV_1% predicted was negatively associated with bronchial wall thickening and consolidation while KCO% predicted was negatively associated with the total emphysema score. Bronchiectasis was minimal in all groups.

Abreviations: COPD, Chronic obstructive pulmonary disease; FEV_1, Forced expiratory volume in 1 s; FVC, Forced vital capacity; HRCT, High resolution computed tomography; ICS, Inhaled corticosteroids; NA, Neutrophilic asthma; SC, Smoking controls; TCC, Total cell count.

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Conclusion: The pattern of radiographic lung abnormality in neutrophilic asthma differs significantly from COPD, and resembles asthma. Neutrophilic asthma is a distinct inflammatory subtype of asthma with a different pathogenesis to COPD.

Introduction

Asthma is an obstructive airway disease characterised by an abnormal and heterogeneous airway inflammatory response. In addition to the allergen driven, corticosteroid sensitive eosinophilic pattern, many patients exhibit a noneosinophilic form of the disease that is relatively resistant to inhaled corticosteroid therapy.[1–3] Neutrophilic asthma (NA) is present in about 20–30% of asthmatics and is characterised by an intense neutrophilic bronchitis and dysfunction of the innate immune system.[4] The consequences of this response may be airway wall remodelling. Remodelling is well described with eosinophilic airway inflammation,[5] where the changes can be detected by high resolution computed tomographic (HRCT) scanning and include bronchial wall thickening, mosaic lung attenuation, and mucus plugging.[6,7] It is unclear if there are structural airway changes in neutrophilic asthma.

Chronic Obstructive Pulmonary Disease (COPD) is an obstructive and inflammatory airway disease typically with increased neutrophils and like NA; it is more common in older people. COPD is accompanied by well-established structural pulmonary changes. Typically this is emphysema, but bronchiectasis and bronchial wall thickening have recently been recognised to occur in COPD.[8,9] Since there are similarities in the demographic profile and inflammatory response between NA and COPD, it has been suggested that NA may be a form of COPD. If this was the case, then there would be similar structural changes in NA and COPD.

The purpose of this study was to examine pulmonary airway and parenchymal changes in NA and COPD using HRCT of the chest. Since smoking can modify the inflammatory response, a group of smoking controls without known airway disease were included for comparison. We tested the hypothesis that NA was associated with a distinctly different pattern of HRCT abnormality to COPD and smoking controls.

Methods

Participants

Participants with NA ($n = 10$), COPD ($n = 17$) and smokers without diagnosed airway disease (SC; $n = 8$) were recruited from the Ambulatory Care Service at John Hunter Hospital and by advertisement (SC). The participants with NA and COPD had stable symptoms and treatment, and no exacerbation or treatment changes in the 4 weeks prior to enrolment in the study. The participants with NA met American Thoracic Society criteria for asthma diagnosis[10] and had current asthma symptoms, airway hyperresponsiveness to 4.5% saline, and increased sputum neutrophil counts (>61%).[1] The participants with COPD had incomplete reversibility of airflow obstruction with post-bronchodilator $FEV_1 < 80\%$ predicted and FEV/VC ratio <0.7.[11] They had no history of asthma and a significant past smoking history. The smoker controls were current or exsmokers with no diagnosed respiratory disease, no treatment and no airflow obstruction. All participants were stable (no lower respiratory tract infection or exacerbation of respiratory disease in the previous 4 weeks) at the time of assessment.

Design

Participants attended for 2 study visits. At the first visit, written informed consent was obtained followed by clinical assessment, spirometry, gas diffusion studies, combined hypertonic saline challenge and sputum induction as well as a skin allergy test. Participants then attended a second visit for chest HRCT. The Hunter Area Health Service and The University of Newcastle Research Ethics Committees approved this study.

Chest CT

HRCT of the chest was obtained using Cardiac 64 multislice scanner (Siemens, Germany). Sections of 1 mm thicknesses were obtained at 10 mm intervals in full inspiration and in expiration. A high spatial resolution algorithm was used and images were photographed at appropriate window settings (lung window: level −700 HU; window 2000 HU). Scans were scored independently by a thoracic specialist radiologist (D.G.M.) blinded to the subject group using a modified Bhalla scoring system as previously described.[12] Both inspiratory and expiratory scans were scored. Each of six lobes was scored (the lingula was regarded as a separate lobe) at inspiratory CT scanning, as previously described,[13] using a modification of the Bhalla system.[14] Air trapping was evaluated. The presence and extent of bronchiectasis, on the basis of established CT criteria,[15,16] were scored as follows: grade 0 = no disease; grade 1 = localised bronchiectasis affecting one or part of one bronchopulmonary segment (localised); grade 2 = bronchiectasis in more than one bronchopulmonary segment (extensive); grade 3 = generalised cystic bronchiectasis. The average severity of bronchial dilatation was quantified relative to the adjacent pulmonary arteries as follows: grade 0 = no bronchiectasis; grade 1 = 100–200% arterial diameter; grade 2 = 200–300% arterial diameter; grade 3 = >300% arterial diameter. Bronchial wall thickness was quantified relative to the adjacent pulmonary arteries as follows: grade 0 = none; grade 1 = <50% arterial diameter; grade 2 = 50–100% arterial diameter; grade 3 = >100% arterial diameter. The presence or absence of mucus within the large airways and (separately) within the centrilobular bronchioles was recorded.