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THE PATHOGENIC ROLE OF ELASTASE IN BRONCHIECTASIS

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Elastase is present in sputum and bronchial secretions of patients with COPD and bronchiectasis. Elastase digests elastin, basement membrane collagen and proteoglycan in the connective tissues of the lung and could lead to severe lung damage. Recent studies have suggested roles for pro-inflammatory mediators, chronic bacterial infection, and elastase activities in the pathogenesis of bronchiectasis. However, the clinico-pathological correlation of elastase has not been studied in a quantitative manner. We have therefore recruited 30 patients (17F; 48.5±16.5 yrs; FEV_1/FVC 1.3±0.6/2.1±0.9) who had steady state bronchiectasis prospectively. Elastase levels in sputum sol was obtained by determining the rate of change in optical density of succinyl-L-alanyl-L-alanine-p-nitroanilide and comparing with standard curves. Freshly produced sputum was serially diluted and cultured quantitatively on enriched and selective agars, and examined by using haemocytometry for leukocyte density. Sputum sol interleukin (IL)-1β, IL-8, tumor necrosis factor (TNF), and leukotriene (LT) B4 were measured using ELISA techniques. There was a correlation between elastase levels with 24h sputum volume (r=0.62, p=0.0003), FEV_1 (-0.45, 0.01), FVC (-0.52, 0.003), exacerbation frequency (0.39, 0.03), and number of bronchiectatic lung lobes (0.63, 0.0003). In addition, elastase also correlated with sputum leukocyte density (0.53, 0.003). There was, however, no correlation between the sputum leukocyte density and inflammatory mediator concentrations with sputum bacterial densities (p>0.05). Our results suggest that elastase in fact plays a more clinically significant role in the pathogenesis of bronchiectasis. These findings could re-conceptualize the treatment of bronchiectasis.

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ENDOTHELIN-1 IN THE PATHOGENESIS OF STABLE BRONCHIECTASIS

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Endothelin-1 (ET-1), originally derived from cultured endothelial cells, is one of the most potent vasoconstrictors. In addition, ET-1 has also been found to have a wide range of biological activities. ET-1 enhances neutrophil adhesion to endothelial cells, promotes neutrophil migration, and activates neutrophils to cause tissue damage which also occur in bronchiectasis. Although there are distinct inflammatory element in the pathogenesis of bronchiectasis, the precise mechanisms are unclear. We hypothesized that ET-1 might contribute to neutrophil recruitment in the tracheobroncial tree of bronchiectasis and therefore augment the airway damage. In this study, ET-1 levels in the serum and sputum sol were measured in 32 clinically stable bronchiectasis patients and 9 control subjects by commercial available ET-1 ELISA kit (Amersham, U.K.). The serum ET-1 was markedly raised in severe bronchiectasis, particularly in the presence of chronic infection by *Pseudomonas aerugunosa (P.A)* (28 pg/ml, range 9.7-136), compared with non-*P.A.* infected patients (8.4 pg/ml, range 0-36.4, p<0.05) and controls (8.4 pg/ml range 0-61.2, p<0.05). No significant difference were found in the sputum sol ET-1 between *P.A.* infected and non-*P.A.* infected brochiectasis patients (p>0.05). Our pilot results appear to have identified a possible pathogenic role for ET-1 in bronchiectasis. Further studies on the clinico-pathological correlation and expression of ET-1 are underway to evaluate this potentially important role of ET-1 further.

This abstract is funded by: Respiratory Research Fund of the University of Hong Kong