Live and let die: is neutrophil apoptosis defective in severe asthma?

Helen Parfrey, Neda Farahi, Linsey Porter, Edwin R Chilvers

Patients with severe asthma make up a relatively small proportion of the total population of patients with asthma yet account for a disproportional amount of asthma-related morbidity and healthcare utilisation.1 2 These patients are usually highly symptomatic, difficult to treat and can be extremely refractory to current treatments. As a consequence, understanding the mechanisms underlying this particular form of asthma is of paramount importance.

Morphological examination of the asthmatic airway reveals epithelial desquamation, thickening of the reticular basement membrane, mucus gland hyperplasia, goblet cell differentiation, angiogenesis and smooth muscle hypertrophy.3 In addition to these structural changes, an inflammatory cell infiltrate is evident within the airways comprising eosinophils, mast cells, lymphocytes and neutrophils. While eosinophils are the most characteristic inflammatory cell type present in mild to moderate asthma, the neutrophil seems to take centre stage more often in patients with severe disease. In fact, the neutrophil is one of the earliest inflammatory cells recruited to the airways following allergen exposure and is particularly evident in bronchoalveolar lavage samples and bronchial and transbronchial biopsies from patients with

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corticosteroid-resistant asthma, occupational asthma and fatal asthma as well as those with acute exacerbations. Furthermore, measures of asthma severity such as forced expiratory volume in 1 s correlate directly with the number of neutrophils present in the sputum and bronchial wall. There is also evidence of neutrophil activation and impaired function in the asthmatic airway. Moreover, neutrophil elastase is recognised to be highly histotoxic and results in epithelial and eosinophil activation, increased vascular permeability and promotion of transforming growth factor β release which is linked to airways remodelling.

Given the propensity of neutrophils to die quite readily by ‘constitutive’ (ie, inbuilt time-dependent) apoptosis when studied in vitro, one major puzzle in inbuilt time-dependent apoptosis when which is linked to airways remodelling. The presence of eosi

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context of severe asthma. Identifying the neutrophil survival factor(s) present in this patient group is clearly an important next step and, if targetable, may form the basis of a new therapeutic approach for this difficult-to-treat patient group.

While this study provides further evidence that neutrophil apoptosis may be deregulated in severe asthma, a number of key questions remain. We need to understand the dynamics of cell migration into and out of the airway wall and determine the true residency times and the relative contribution of apoptosis and, indeed, other non-apoptotic death mechanisms such as autophagy, NETosis20 and cytolsis in granulocyte clearance. We also need to understand the signals that block apoptosis in the airway wall (yet seemingly not in the airway lumen) and to determine what drives the switch from eosinophil- to neutrophil-dominated inflammation. Drugs which target the removal rather than the arrival of granulocytes in tissues are now emerging,29 and such agents may offer an important adjunct to current asthma treatments.

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British Thoracic Society Pleural Disease Guidelines - 2010 update

Nick Maskell, on behalf of the British Thoracic Society Pleural Disease Guideline Group

INTRODUCTION

Pleural disease remains common, affecting over 3000 people per million population each year. It therefore presents a significant contribution to the workload of respiratory physicians. These guidelines attempt to summarise the available evidence to aid the healthcare professional in delivering good quality patient care.

AIMS AND OBJECTIVES OF THE GUIDELINE

Since the last BTS pleural disease guidelines were published in 20033 a large number of good quality primary research papers have been published and the guidelines need to reflect this new data. In addition, there was a need to develop new sections on local anaesthetic (LA) thoracoscopy and thoracic ultrasound to reflect changes in clinical practice.
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