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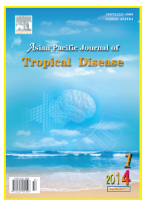

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The importance of eosinophil, platelet and dendritic cell in asthma

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PEER REVIEW

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Comments

This is a good study in which the authors stated the importance of eosinophil, platelet, and DC in asthma and future of treatment. The data are interesting. The results can be used in the treatment and control of asthma.
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ABSTRACT

Asthma is a syndrome of variable airflow obstruction. It is characterized pathologically by bronchial inflammation and remodeling changes. Eosinophil infiltrate in asthma and a relationship between the degree of eosinophil infiltration in airways and severity of asthma has been suggested. Eosinophil has antigen-presenting cells and main role in allergic asthma. Platelets in inflammatory response is very important. It has also been shown that enzymes released by activated platelets play a direct role in the chronic inflammatory events that lead to airway remodeling in asthma. Dendritic cells (DCs) acquire antigen in the airways and then migrate to the draining lymph node where the cells mature and initiate T cell responses. Allergen challenge induces simultaneous increases in the number of DCs in the lungs. Because DCs are crucial in mounting immune responses during ongoing inflammation in the lung and balance of the allergic immune response.

KEYWORDS

Allergic asthma, Eosinophil, Platelet, Dendritic cell

1. Introduction

Asthma is a chronic respiratory problem characterized by recurring attacks of impaired breathing, of varying intensities. The definition of asthma has four cardinal components which are bronchoconstriction, symptoms, airway inflammation, and airway hyper-responsiveness. Few new drugs representing novel modes of action have been introduced over the last 30 years[1-3]. Indeed the mainstays of treatment, in the form of inhaled corticosteroids, b2 adrenoceptor agonists and cholinergic antagonists, were first used clinically[4,5]. None of these drugs prevent asthma. The goal of therapy is two-fold to limit the current impairment or symptoms, and to reduce the risk for a severe attack in the future. Since even patients with mild asthma have evidence for inflammation of the large and small airways, and the severity of the inflammation often correlates with the severity of the disease[6-8]. The cellular pathology, recognition receptors, co-stimulatory molecules, key transcription factors, cytokines, chemokines, adhesion molecules, and other mediators, have been investigated and incorporated into a comprehensive, detailed, unifying model of the events that translate into asthma[9-11].

2. Mechanisms of asthma

Asthma is a syndrome of variable airflow obstruction. It is

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characterized pathologically by bronchial inflammation and remodeling changes, physiologically by bronchial hyper-responsiveness, and clinically by cough, chest tightness and wheeze. Cytokines secreted by CD4+Th2 type T cells play a major role in allergic asthma and other effectors cells, such as myofibroblasts, epithelial cells, smooth muscle cells and endothelial cells, which play an intermediary role in airways damage and remodeling[12-15]. Etiological trigger factor for asthma is exposure to environmental antigens, in particular inhaled allergens, including occupational allergens and infectious agents, which are probably a major drive to T cell activation in asthma. Genetic factors governing the production of T cell cytokines and their actions on target cells, as well as variability in the structure and development of the mesenchymal elements of the bronchial mucosa influence the risk of developing asthma[16-18].

3. Eosinophil function in asthma

Eosinophils are suspected in the inflammatory infiltrate in asthma and a relationship between the degree of eosinophil infiltration in airways and severity of asthma has been suggested. The severity of asthma correlates with levels of circulating and bone marrow eosinophils, and the evaluation of asthma has usually involved determination of eosinophil counts[19-21]. Eosinophil-derived cationic proteins are also detectable in plasma of asthma patients. Eosinophils, through their release of basic proteins and lipid mediators, are strongly implicated in mucosal damage and involved in mechanisms that underlie bronchial hyperreactivity. When asthma is under remission due to corticosteroid therapy, levels of circulating eosinophils plummet[19-22]. Asthma patients develop a low density population of circulating eosinophils. Large numbers of eosinophils are recoverable from sputum and bronchoalveolar lavage of asthma patients, and the levels of eosinophils correlate with the severity of asthma. Circulating IL-5 is often detectable in asthma patients[23-25]. The histopathology of asthma shows massive infiltration of the bronchial mucosa by eosinophils and other inflammatory cells and an associated deposition of eosinophil granule cationic proteins. This is associated with structural changes that include damage to or loss of ciliated epithelial cells, thickening of the basement membrane, and the accumulation of mucus and debris[26,27].

Bronchial associated eosinophils have physical and functional characteristics that demonstrate a state of activation, which include reducing density and elevating protein kinase C activity. There are several direct mechanisms by which eosinophils may cause disease. The toxicity of eosinophil cationic proteins and oxygen metabolites may be responsible for the damage to ciliated cells and the desquamation of the tracheal epithelium that is observed with the disease. Major basic protein (MBP) induces airway smooth muscle constriction and hyperresponsivenessin. Pulmonary parasympathetic nerves release acetylcholine, which binds smooth muscle M3 muscarinic receptors and stimulates bronchoconstriction. Acetylcholine release is self-regulatory by a mechanism that involves binding to M2 muscarinic receptors on the nerve endings. It was found that MBP inhibits the binding of the drug N-methylscopolamine to M2 but not M3 receptors. This shows that MBP alters the binding properties of the inhibitory M2 receptor and have the potential to block the feedback suppression of acetylcholine release[28-30].

The eosinophil has the greatest capacity for leukotriene C4 (LTC4) synthesis of any cell associated with inflammation. LTC4 can induce smooth muscle constriction and microvascular permeability. This substance is thought to contribute to the stromal fibrosis and basement membrane thickening that is observed in this asthma. This mechanism may also produce similar changes in asthma. In addition to these direct mechanisms for the induction of hyperresponsiveness and bronchoconstriction, eosinophils have the potential to make indirect contributions by the production of mediators that stimulate the functions of other inflammatory cells[31-34].

4. Eosinophilic airway inflammation in bronchial asthma

Eosinophils preferentially accumulate at sites of allergic inflammation and are believed to play important roles in the pathophysiology of asthma through the release of a variety of inflammatory mediators, including MBP, cysteinyl leukotrienes (CysLTs), radical oxygen species, and cytokines[35-37]. In asthmatic patients with persistent sputum eosinophilia, treatment with anti-IL-5 mAb reduced asthma exacerbations and the requirement for systemic corticosteroids, and improved asthma-related quality of life. These results strongly suggest essential role of eosinophils in the development of asthma exacerbation. Furthermore, antagonizing IL-5 could be an effective strategy for controlling refractory eosinophilic asthma as well as controlling hypereosinophilic syndrome[5,38-40]. Eosinophils largely contribute to the development of airway remodeling of asthma. During the season for pollen allergy, however, only eosinophils, but not mast cells or macrophages, express LTC4 synthase in the bronchial tissue. So eosinophils are a major cellular source of CysLTs in asthma. For circulating eosinophils to accumulate in asthmatic airways, they must adhere to and then migrate across vascular endothelial cells. These processes are largely regulated by cytokines/chemokines produced by a variety of cells, including Th2 cells[41,42]. Accumulating evidence has suggested that