ALLERGIC INFLAMMATION AND PLATELET ACTIVATION: A KEY FOCUS TO ASTHMA

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ABSTRACT

Asthma is defined as a chronic inflammatory lung disease that is characterized by airway hyperactivity, eosinophil inflammation, and mucus hypersecretion resulting in intermittent airway obstruction. Inflammation and immune reactions are indeed believed to start as time- and site specific defence mechanisms. Failure to resolve an acute beneficial response could later lead to a vicious and anarchic state of chronic activation, which causes healthy tissue damage. Blood platelets, apart from their traditional and well-recognised function in haemostasis, play an essential and active role in allergic inflammation e.g. through their participation in cell recruitment from blood to site of immune reactivity as a result of direct interactions with leukocytes, and through the release of inflammatory mediators. Platelet activation may occur during human allergic reactions both systemically and locally at the site of allergic inflammation as a result of an IgE-dependent process and as a secondary event caused by other inflammatory or immune stimuli.

Keywords: Asthma, Inflammation, immune system, Platelet

INTRODUCTION

Inflammation and immune reactions are indeed believed to start as time- and site specific defence mechanisms. Failure to resolve an acute beneficial response could later lead to a vicious and anarchic state of chronic activation, which causes healthy tissue damage. To avoid excessive collateral tissue damage, therefore, the tissue may release a second danger signal that can evoke anti-inflammatory responses. This second danger signal indicates the danger from overactive immune cells and would trigger the down regulation of the proinflammatory activities of the immune system to prevent destruction of healthy tissues. Inflammation is a complex reaction of host defence mechanisms aiming at neutralization of an insult and restoring normal tissue structure and function. A key pathological event in an acute phase of many forms of inflammation is the recruitment of polymorphonuclear leukocytes in response to a perceived pathogen. This is especially important for innate immunity, which provides the first and fast line of defence for the host. The molecular mechanisms that orchestrate the influx of neutrophils to the site of inflammation are not entirely clear. It is now believed that cells traditionally viewed as those associated with adaptive immunity and tolerance, such as T lymphocytes, may also significantly contribute to and modulate the course of inflammatory reaction [1-4].

Asthma is defined as a chronic inflammatory lung disease that is characterized by airway hyperreactivity, eosinophil inflammation, and mucus hypersecretion resulting in intermittent airway obstruction [5]. The aetiology of asthma is complex

and multifactorial; development of the disease is controlled by both host genetic factors and a variety of environmental exposures. Although environmental influences, particularly a decrease in infections because of improved hygiene, might have increased allergic diseases, at least a dozen polymorphic genes have been calculated to regulate asthma, by controlling the inflammatory response, immunoglobulin E (IgE), cytokine, and chemokine production, and airway remodelling [6,7,8]. This study reviews on the

ROLE OF PLATELETS ON INFLAMMATION

There is an increasing amount of evidence to prove that platelet, apart from their well-recognised role in haemostasis, participate in inflammatory reactions, including allergic inflammation. In this role platelets may not be accessory cells; instead they may participate directly in allergic disorders. Allergens specific IgE-mediated platelet activation in allergic disorders has been suggested. Human platelets could interact with IgE antibodies through a specific membrane receptor for IgE. It has been demonstrated that both, low affinity receptor (Fc(RII) [9,10] and the high affinity receptor (Fc(RI) for IgE [11, 12] are expressed on the cell surface of human platelets. In atopic asthmatics, the percentage of platelets that bound IgE was markedly higher compared to normal donors, and such platelets could be directly activated by contact with the corresponding allergen [13]. Therefore, allergen-specific IgE-mediated platelet activation in allergic disorders has been suggested. In addition, it has been shown that activation of human platelets via the Fc (RI induces release of platelet-derived mediators such as serotonin and cytokines e.g. RANTES [14]. On the other hand, DeSousa et al. [15] postulated that platelet reactivity to allergen contact must be an expression of multi cellular interaction rather than direct effect on platelet IgE receptor stimulation. Moreover, it has been demonstrated that platelets can be activated through direct contact with T cells, and through the release of RANTES, a b-family chemokine containing the CC motif, recruit secondarily more T cells, leading to further platelet activation [16]. The results point to the existence of a novel platelet dependent pathway to amplify the immune response, bringing therefore platelets close to the level of pathogenic relevance, traditionally attributed to classical immune cells [16].

Platelets show the capacity to get activated upon local and systemic allergic reactions. The degree of platelet activation can be evaluated by measurement of plasma concentrations of specific platelet proteins or by quantification of surface receptor expression. Upon activation platelets secrete different biologic mediators with potent inflammatory properties, of which beta-thromboglobulin (b-TG) and platelet factor 4 (PF-4) are considered to be important markers of platelet activation process in vivo [17]. b-TG and PF-4 belong to the platelet family of proinflammatory cytokines named chemokines, which are responsible for accumulation and activation of leukocyte populations at inflammatory sites. These chemokines and other platelet-derived, biologically active mediators are considered to be the pathogenic factors in allergic diseases [10, 11].

In vitro studies have shown that activated human platelets release a soluble factor or factors that may induce histamine release from mixed leukocytes containing basophilis [12]. Suzuki et al. [13] showed that PF-4 fragment stimulates, in a dose dependent manner, histamine release from peritoneal mast cells suggesting that this chemokine may play a crucial role at the site of inflammation and/or immune response. Pitchford et al. [14] observed circulating platelet-leukocyte aggregates in the blood of allergic asthmatics during allergen-induced late asthmatic response and in sensitized mice after allergen exposure, suggesting an essential role for platelets in leukocyte blood to tissue trafficking in allergic inflammation. Knauer et al. [15] demonstrated elevated PF-4 level in the circulation of asthmatic subjects after ragweed extract

bronchoprovocation. The association of PF-4 with the onset of changes in forced expiratory volume within one second (FEV1) suggests that platelet activation occurred at the time of the allergic response and was the result of the mediator release from the lung [16]. Moreover, increased intravascular platelet activation was observed during late allergic response in house dust mite allergic asthma patients undergoing bronchial allergen challenge [17]. In asthmatics, the defective release of PF-4 has been detected in vitro [18], probably reflecting increased platelet degranulation in vivo. Interestingly, Pareti et al. have suggested that platelet dysfunction in vitro may be related to the presence of exhausted platelets in the circulation, following their in vivo over stimulation [19]. Taytard et al. investigated platelet kinetics and sequestrations in asthmatic patients free of any clinical symptoms. The platelet survival curve (radioactivity degradation) showed a biexponential decay pattern, whereas in normal subjects, the curve was monoexponential, suggesting the presence of two highly distinctive populations: one of a short life span (rapidly degrading population) and another of a normal life span. These results suggest the presence of functional or anatomic lesions of platelets in asthmatic patients [20]. Moreover, platelet activation may be a factor in airway remodelling, which is one of the consequences of persistent, chronic inflammation in asthma. It has been demonstrated that blood platelets are essential for structural remodelling in a murine model of chronic allergic airway inflammation [21].

The fact that blood platelet may be activated and actively participate in allergic inflammation associated with asthma raises the question whether enhanced activity of platelets occurs in other clinical manifestations of atopy, such as allergic rhinitis and atopic eczema/dermatitis syndrome (AEDS). AEDS is a chronic inflammatory disease, characterised by an exacerbating and remitting course. Specific IgE is involved in the clinical response to allergens in IgE-associated variants of AEDS [22].

Allergic rhinitis is the most common of atopic diseases strongly associated with asthma. From the pathophysiological point of view, both bronchial asthma and allergic rhinitis are mediated by similar allergic inflammatory mechanisms. However, there is no evidence of any increased activity of circulating platelets as marked by b-TG and PF-4 in symptomatic patients with grass-induced seasonal allergic rhinitis, at the peak of the allergy season [23].

The platelet derived chemokines may be involved in the recruitment and activation of inflammatory cells, including eosinophils, contributingmthereby to pathogenesis of AEDS associated skin inflammation. Eosinophil is considered an important effector cell in AEDS. It has been demonstrated that eosinophils from the circulation of patients with AEDS exhibit potentiated migratory response towards PF-4, compared with eosinophils from normal donors [24]. Hayashi et al. [17] suggested that PF-4 not only modulates chemotactic activity of eosinophils, but also intensifies the function of eosinophil adhesion. PF-4 may be a molecule responsible for induction of eosinophils towards ulcerative skin lesions characteristic for this disease [25].

Platelets are implicated within a wide range of physiological roles in haemostasis. Moreover, they can function as inflammatory cells involved in allergic disorders. There is an increasing body of evidence to prove that blood platelets contribute to intensification, maintenance, and regulation of inflammatory reactions, including allergic processes.

CONCLUSION

Data concerning platelet activity in allergic diseases are not consistent. It is interesting to speculate that platelet may be differently involved in allergic processes in patients with different forms of allergy. It

seems likely that differences exist in platelet reactivity itself, including releasability of platelet products between patients with various clinical manifestation of atopy. Platelet activation may occur during human allergic reactions both systemically and locally at the site of allergic inflammation as a result of an IgE-dependent process and as a secondary event caused by other inflammatory or immune stimuli. Altered platelet function as measured by platelet secretion, expression of surface molecules, aggregation, adhesion or arachidonic acid metabolism has been found in patients suffering from allergic diseases.

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