The role of intrapulmonary and Serum Complement Component 5 (C 5)in the pathogenesis of atopic asthma

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Submitted By

Hosam Eldean Mahmoud Fawy

M.B,B.CH.

Supervised by

Professor Doctor / Mohamed Kamel Sabry
Prof. of Allergy & clinical immunology
Faculty of medicine
Ain Shams university

Professor Doctor / Mohamed Abdelrhaman El shayeb
Prof. of Allergy & clinical immunology
Faculty of medicine
Ain Shams university

Doctor / Eman Alsayed Ahmed
Lecture of internal medicine
Faculty of medicine
Ain Shams university
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List of abbreviation

ADAM33	**A D**isintegrin**A**nd **M**etalloproteinases
AHR	Airway hyperresponsivness
AP	Alternative pathway
ATS	Anaphylatoxines
BAL	Broncho-alveolar lavage
C1	Complement component 1
C2	Complement component 2
C3	Complement component 3
C4	Complement component 4
C5	Complement component 5

C6	Complement component 6
C7	Complement component 7
C8	Complement component 8
C9	Complement component 9
IgE	Immunoglobuline E
MAC	Membrane attack complex
MBL	Mannose binding lactine
PAMPS	Pathogen associated molecular pattern
PRRS	Pattern recognition receptors

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Introduction

Asthma is characterized by a combination of chronic airway Inflammation, airway obstruction, and airway hyperresponsiveness (A H R) to various stimuli. It is though to be mediated primarily by adaptive immune responses mediated by allergen- specific CD4 T cells, Th2 cytokines, and allergen specific IgE, which lead to pulmonary inflammation and AHR (Peng et al., 2005).

Nagy and coworkers had found that Complement and its activated components , which from a central core of innate immune defense against bacterial, viral , and fungal invasions, can be activated through the classical pathway, the alternative pathway , and the lectin pathway (Nagy et al.,2003).

All three activation pathways converge at complement Component C5 prior to the generation of C5a and C5b-9, both of which induce potent biological responses, including tissue injury, inflammation, anaphylatoxic responses, and cell lyses at very low

concentrations (Takafuji et al., 1994) In addition , C5 can be activated after allergen exposure (Nagata et al., 1987)

Recent data from animal models of allergic asthma suggest that activated complement components, such as C5, provide a critical link between innate and adaptive immunity (Karp et al., 2000.)

Several experimental models for bronchial asthma have indicated that C5 and its activated components are involved in the development of airway inflammation and bronchoconstriction. Studies with various complement inhibitors markedly reduced AHR or airway inflammation in rodents (Lukacs et al.,2001) . The potential involvement of C5 activation was also extended to clinical observations that the severity of clinical symptoms was correlated with the extent of C5 activation.

On the other hand , studies have shown that C5 deficiency leads to increased susceptibility to allergen – induced AHR in mice, and this finding is supported by

evidence of decreased production of Il-12 , a key Th1 cytokine reported to modulate the pathogenesis of asthma (Karp et al.,2000).

The key question at the center of the debate is whether C5 ant its activated components are pro-inflammatory or anti-inflammatory during the sensitization phase and the effector phase of the pathogenesis as suggested , respectively , by studies of C5 deficient (C5d) animals (Karp et al., 2000) and experiments involving intervention during the course of disease (Abe et al., 2001) Another key issue is whether Intrapulmonary activated complement components play a significant role in the pathogenesis and overcome the potential anti- inflammatory effect of activated C5 components on the adaptive immune system (Karp et al., 2000) .

However, controversies remain regarding the involvement of C5 and its activated components in the pathogenesis of asthma (Gerard et al., 2002).

Aim of the Work

This study is designed to evaluate the role of complement C5 both intrapulmonary and in the serum in atopic asthma.

Asthma

Definition of asthma :

Asthma is defined by GINA. , 2008, as follows:

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role.

The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.

Epidemology of asthma:

Asthma is a problem worldwide, with an estimated 300 million affected individuals.