Production of Interleukin-5, Interleukin-13 and Interferon-γ in Peripheral Blood CD8+ T Cells from Children with Wheezing

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Abstract

Purpose: Our objective was to investigate the role of CD8+ T cells in pathogenesis of wheezing in children with atopic nature.

Methods: Twelve atopic wheezers, 8 nonatopic wheezers, 8 disease controls and 8 healthy controls were enrolled in the study. We isolated CD8+ T cells from peripheral blood samples, incubated them for 72 hours either in the absence or presence of phytohemagglutinin (PHA) and compared the concentrations of interleukin (IL)-5, IL-13, and interferon (IFN)-γ in the cell culture supernatants.

Results: In the atopic wheezer group, the IL-5 concentration was significantly higher after PHA stimulation than after non-stimulated incubation. This difference was not observed in the nonatopic wheezer, disease control and healthy control groups. IL-13 was undetectable in all of the cell culture supernatants. There was no significant difference in the IFN-γ concentration between the PHA-stimulated and non-stimulated conditions in all 4 groups.

Conclusion: The results of this study suggest that CD8+ T cells may play a role in the pathogenesis of wheezing in children with atopic nature through the production of IL-5.

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Key Words: CD8+ T cell, Interleukin-5, Interleukin-13, Interferon-γ

Introduction

Wheezing is a whistling sound produced by the passage of air through narrowed airways during expiration and it is most frequently heard in infants and young children during viral respiratory infections or asthma exacerbations. Other conditions leading to wheezing include anatomic airway abnormalities, immunodeficiency, mucociliary clearance disorders, bronchopulmonary dysplasia, and aspiration syndromes.1) Nearly half of all children experience at least one episode of wheezing by the age of six.2)

The clinical and epidemiologic aspects of the various wheezing episodes in young children differ from those in older children and adult asthmatics. However, asthma-like inflammatory responses, such as increased
number of inflammatory cells and thickening of the alveolar basement membrane, may be observed in wheezy infants. This observation may imply that there are common immunologic mechanisms underlying asthma and certain conditions that produce wheezing in children.

Traditionally called cytotoxic T cells, the classic role of CD8+ T cells is to function in the host defense against pathogens, especially viruses: CD8+ T cytotoxic-1 (Tc1) cells are activated in viral infections and produce interferon (IFN)-γ and lymphotoxin. The relatively novel role of CD8+ T cells is in contributing to airway inflammation in allergic patients: CD8+ T cytotoxic-2 (Tc2) cells can produce interleukin (IL)-4 and IL-5, stimulate eosinophil recruitment, and help B cells produce immunoglobulin E (IgE) when induced in the presence of IL-4. It has been theorized that some viruses cause an allergic response in the airway by inducing CD8 Tc2 responses.

The effects of T lymphocytes are mediated in large part through the action of cytokines, and the functions of several cytokines in allergic reactions are well established. IL-5 is an important cytokine in the pathogenesis of allergic reactions. It induces the production, activation, and chemotaxis of eosinophils. In addition, the administration of IL-5 has been shown to cause mucosal eosinophilia and bronchial hyperreactivity. IL-13 is another proinflammatory cytokine which induces isotype switching in B cells to the IgE isotype. Conversely, IFN-γ decreases allergic responses by inhibiting the IL-4-mediated secretion of IgE.

In this study we sought to find whether CD8+ T cells, which are known to be involved in airway inflammation in allergic patients, are also involved in the pathogenesis of wheezing in children with atopic nature. For this purpose, we compared the cytokine production upon phytohemagglutinin (PHA) stimulation of peripheral blood CD8+ T cells isolated from atopic and nonatopic wheezers.

Methods

1. Subjects

Children with the chief complaint of wheezing who were admitted to Kangnam St. Mary’s Hospital from July 1, 2006, to June 30, 2007, were included. (Table 1, n= 20). Specific IgEs to Dermatophagoides pteronyssinus, Alternaria tenuis, cat epithelium, cockroach, egg white, and milk were measured using Uni-CAPT™ (Pharmacia and Upjohn, Uppsala, Sweden). Twelve children showed elevated specific IgE levels for at least one of the allergens and they were classified as atopic wheezers. Eight children showed negative results on the specific IgE tests and they were classified as nonatopic wheezers.

Sixteen children admitted during the same period were included as control subjects. Eight of them had histories of recurrent lower respiratory tract infections without wheezing and they were admitted due to pneumonia (n= 8); they were classified as disease controls. Eight children who were admitted due to noninfectious noninflammatory illnesses (short stature n=1, precocious puberty n=6, chylous ascites n=1) and had no history of