

Effect of immunotherapy on sCD23 levels in patients allergic to Hymenoptera venom

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Background: sCD23 is the designation given to the low affinity IgE receptor. The soluble fragment of this receptor (sCD23) participates in the regulation of IgE synthesis.

Objective: The purpose of this study is to examine the effect of a venom immunotherapy regimen on sCD23 levels.

Methods: We measured sCD23 levels by ELISA in Hymenoptera venom-allergic patients (positive skin tests and a history of systemic reactions to Hymenoptera sting) in serial sera collected over a course of venom immunotherapy with a mean duration of 54 months. Mean pre-sCD23 and post-sCD23 levels were compared using a Student's two-tailed *t* test.

Results: sCD23 levels were found to be unchanged over the course of venom immunotherapy.

Conclusions: This is the first longitudinal study that has been done. It suggests that while both immunotherapy and sCD23 are known to be involved in the regulations of IgE synthesis in the atopic patient, the immunomodulation seen in venom immunotherapy is not mediated through sCD23 in any simple regulatory manner.

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INTRODUCTION

CD23 is the designation given the low affinity IgE receptor (Fc ϵ RII) found on the cell surface of certain B and T lymphocytes, eosinophils, macrophages, and platelets.¹ The soluble fragment of this receptor (sCD23) appears to be identical to IgE binding factor and to participate in the regulation of IgE synthesis,² and therefore, is likely involved in the expression of allergic disease. Elevated levels of sCD23 have been reported in atopic patients.³ The present study was conducted to observe the effect of venom immunotherapy on sCD23 levels in the sera of venom-allergic patients.

It has been well documented⁴ that venom-specific IgE is elevated in venom-allergic patients and in fact, ini-

tially increases over the first few months of immunotherapy with subsequent decrease to a lower baseline level. Given sCD23's purported role in IgE regulation, we hypothesized that a concomitant decrease in sCD23 levels would occur over the course of venom immunotherapy.

METHODS

We measured sCD23 levels in 15 Hymenoptera venom-allergic patients (six females and nine males) determined by positive skin tests to Hymenoptera venom and a history of systemic reactions (including urticaria, angioedema, bronchospasm, hypotension, and laryngeal edema) to Hymenoptera sting. The mean patient age was 38 years (range 12 to 67 years). Serum was collected at initial evaluation as well as serially over the course of venom immunotherapy with a mean duration of 54 months (range 12 to 107 months). Our intent was to examine the influence of an immunotherapy regimen (known to be clinically effective and to

reduce venom-specific IgE levels⁵) on sCD23 levels. We also measured baseline sCD23 levels in ten healthy nonatopic, nonvenom-sensitive volunteers.

sCD23 levels were determined using a sandwich enzyme immunoassay (CELLFREE CD23 Test kit, T Cell Sciences, Inc, Cambridge, MA). Serum samples were added to microtiter wells that had been precoated with anti-CD23 monoclonal antibody. A second anti-CD23 monoclonal antibody, conjugated to an enzyme, was then added. Each of these two distinct monoclonal antibodies is directed at separate distinct epitopes on the CD23 molecule. After unreacted components were removed by washings, a chromogen solution was added that formed a colored product whose absorbance at 490nm was measured. The amount of absorbance measured was proportional to the amount of sCD23 found in the serum sample. CD23 standard solutions were used to prepare a standard curve from which unknown values were determined.

RESULTS

Pre-treatment and post-treatment sCD23 levels in the venom-allergic patients and a group of nonallergic controls are displayed in Table 1. The sCD23 levels pre-immunotherapy and post-immunotherapy were compared using a Student's paired *t* test. No significant difference was observed ($P = .66$) over a protracted course of immunotherapy. There was a trend toward lower sCD23 levels using Student's unpaired *t* test in venom-sensitive patients both pre-treatment and post-treatment as compared with our nonallergic controls. These did not reach statistical significance since pre-treatment sCD23 levels compared with controls resulted in a value of $P = .11$.

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Table 1. sCD23 Serum Levels (units/mL) Pre-Venom and Post-Venom Immunotherapy

	Venom Allergic Subjects (n = 15)		Controls (nonallergic) (n = 10)
	Pre-Immunotherapy	Post-Immunotherapy	
Mean $\pm$ SEM	197 $\pm$ 67	224 $\pm$ 68	403 $\pm$ 82

Graphic representation of the data values is shown in Figure 1. Figure 2 displays the pre-treatment and post-treatment sCD23 values for each of our patients individually.

DISCUSSION

The low affinity IgE receptor (Fc ϵ RII) has been demonstrated on a host of cell types including 90% of IgM, IgD surface-positive lymphocytes. In fact, this receptor has been identified as identical to the B-cell differentiation antigen CD23. While normal non-activated T-cells have virtually no low affinity IgE receptors, certain states of activation promote Fc ϵ RII expression.¹ Parasitic immunity is in part mediated by macrophages that have low affinity receptors that allow for the destruction of IgE-coated schistosomes.⁶ The low affinity IgE receptors have also been shown on monocytes, Langerhans' cells, eosinophils, and platelets. It seems that B cells have a low affinity IgE receptor (Fc ϵ RIIb) structurally different only in the amino terminus of

the molecule from the receptor found in the non-B cells. The expression of Fc ϵ RIIb is much enhanced by elevated levels of IL-4. Both receptors are referred to as CD23, and are functionally equivalent. Fc ϵ RII is not homologous to Fc ϵ RI (the high affinity IgE receptor found on mast cells and basophils) and is not a member of the immunoglobulin gene super family. CD23 is a single 45-kD glycoprotein anchored into the cellular membrane with carboxy terminus found extracellularly. Through a process of autolysis the CD23 receptor degrades into a 37-kD fragment (sCD23) which then goes on to degenerate into even smaller fragments, each with IgE binding ability.¹

Some of the speculation regarding the involvement of Fc ϵ RII in allergic disease is related to the observation that elevated IgE levels are associated with elevated Fc ϵ RII levels.⁷ It also appears that Fc ϵ RII is upregulated by IL-4 and downregulated by gamma-interferon, similar to their effect on IgE production.²

There are several functions that CD23 and its soluble fragments (sCD23) serve. Parasitic immunity is accomplished by the coating of parasites such as *S. mansoni* with IgE. Cytotoxicity and phagocytosis are then mediated by the low affinity IgE receptor found on macrophages and eosinophils.¹ Soluble CD23 is an autocrine B cell growth factor and also potentiates IgE synthesis. Elevated levels of sCD23 have been demonstrated in atopic children as well as adults with allergic rhinitis and asthma.⁷

It has been well established that venom immunotherapy will produce a significant fall in venom-specific IgE in venom-allergic patients. The observation that sCD23 has some role in the regulation of IgE, and its apparent enhanced levels in atopic populations led us to investigate sCD23 levels in the setting of venom-allergic patients receiving immunotherapy.

Yanagihara et al⁸ investigated the influence of immunotherapy on sCD23 levels in aeroallergen-allergic patients. In a cross-sectional study, he compared a group of patients being treated with immunotherapy with a matched group of patients not being treated with immunotherapy. He found no influence of immunotherapy on sCD23. Our results for Hymenoptera-sensitive patients are similar to data published by Yanagihara. The patients in Yanagihara's study with pollen-sensitive respiratory allergy had elevated sCD23 levels compared with non-atopic patients. Our patients, however, had lower mean sCD23 levels (though not statistically significant) when compared with a non-atopic non-venom-sensitive group of control patients.

Although both immunotherapy and sCD23 are known to be involved in the regulation of IgE synthesis in atopic disease, venom immunotherapy is not mediated through an endocrine effect of circulatory sCD23 in any simple, direct regulatory manner. This does not rule out an autocrine or paracrine effect of sCD23.

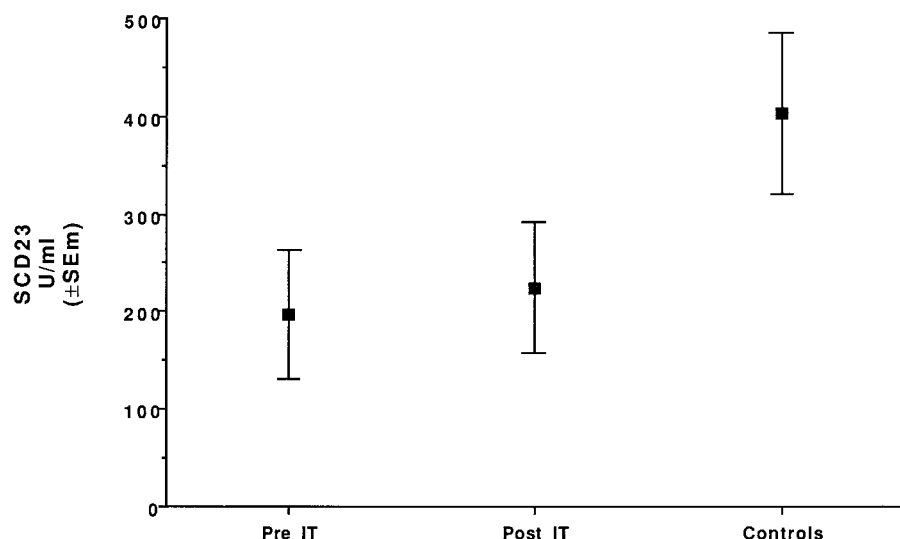


Figure 1. Mean sCD23 levels in patient group (pre-venom and post-venom immunotherapy) and nonallergic controls.

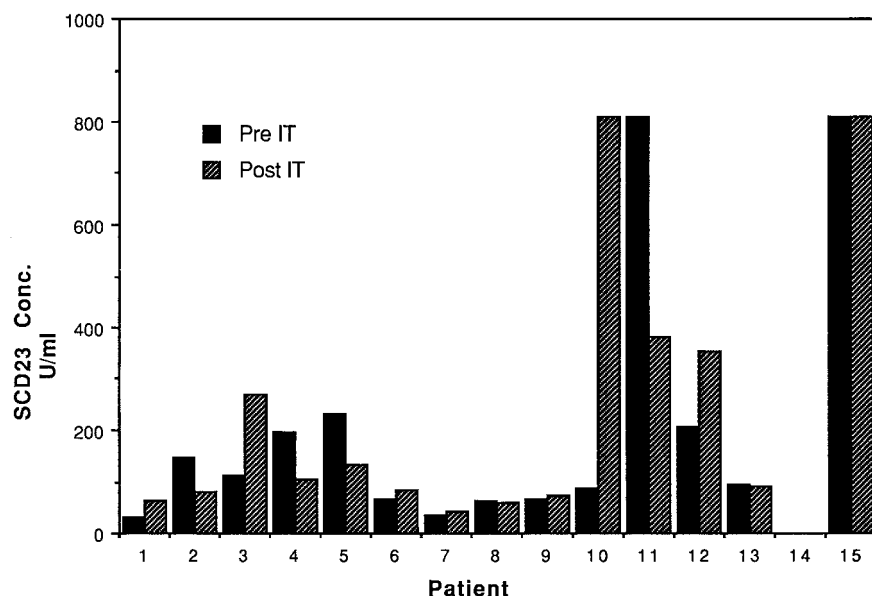


Figure 2. sCD23 levels in individual venom allergic patients pre-treatment and post-treatment.

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