



Soluble CD23 in Allergic Diseases

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Abstract. CD23, a differentiation marker of B cells is identified with the low-affinity receptor for IgE – FcεRII. The CD23 molecule is continuously cleaved by autoproteolysis into soluble fragments called sCD23, considered as a multifunctional cytokine. sCD23 is supposed to play an important role in IgE synthesis. IgE is a hallmark of atopy and its overproduction is a characteristic feature of allergic diseases. The aim of this study was to determine sCD23 (25 kDa) serum levels in patients with inhalant allergy and hymenoptera venom-induced allergy with relevance to IgE system. The trial consisted of 18 patients with pollinosis, 25 with house dust mite allergy and 12 with hymenoptera venom-induced allergy. Eighteen healthy volunteers without signs of atopy served as a control group. Serum levels of sCD23 (25 kDa), total IgE and allergen specific IgE were measured as well. The results were presented as median value, 25–75% range and a total value range. Nonparametric tests (the U Mann-Whitney test, Kruskal and Wallis test and Spearman's correlation rang test) were used. In patients with allergic disorders serum levels of sCD23 were significantly higher than in the control group ($p < 0.05$). No correlation between IgE levels and sCD23 was detected in all the investigated groups. sCD23 does not appear to be a hallmark of allergic diseases, however serum level of that molecule is significantly elevated in patients suffering from allergic disorders. No correlation between sCD23 and IgE has been observed. sCD23 serum level has no relevance to the types of allergic diseases.

Key words: soluble CD23; allergy.

Introduction

Although extensive research during the last decade has provided important data regarding the pathophysiology of allergic disease, the issue still arises many unanswered questions.

IgE is a hallmark of allergy and its overproduction is a characteristic feature of allergic disorders. Recent investigations have identified CD23 antigen as low-affinity receptor for IgE, initially shown as a marker for mature B cells^{11, 13, 20}. The CD23 molecule, identified

on different cell populations, is continuously cleaved by autoproteolysis into soluble fragments¹⁹. The most stable component is the 24 kDa fragment, which is characterized by cytokine-like activities and functional synergy with IL-4 and IL-1¹⁵.

The study was undertaken to estimate sCD23 (25 kDa) serum levels in two groups of patients with inhalant allergy, sensitive to pollens and house dust mite and hymenoptera venom allergy with relevance to IgE system.

Abbreviations used: CD – cluster differentiation, ECP – eosinophil cationic proteins, FAST – fluoroallergosorbent test, FcεRII – low-affinity receptor for IgE, IgE – immunoglobulin E, IL – interleukin, LTB₄ – leukotriene B₄, PAF – platelet activating factor, PGF₂ – prostaglandin F₂, sCD23 – soluble form of CD23.

Materials and Methods

Patients. The trial consisted of 73 age and sex-matched patients (31 men and 42 women, age ranged from 16 to 55 years, mean 30.8). All the patients were divided into 4 groups:

P – with pollen allergy suffering from seasonal allergic rhinitis (18 patients),

D – with house dust mite allergy suffering from perennial allergic rhinitis (25 patients),

I – with hymenoptera venom allergy (12 patients),

C – 18 healthy controls without signs of atopy.

All the subjects were attending the adult out-patient clinic at the Department of Allergology of the Silesian School of Medicine.

The characteristic of the patients is described in Table 1. Selection criteria for all groups were the following: positive history of allergy and positive skin prick tests with relevant allergens. At the time of the study, the symptoms of the disease were controlled using appropriate therapy (antihistaminica, local corticosteroids, local vasoconstrictors and cromoglycates). None of the patients received systemic corticosteroids during the last 3 months or specific immunotherapy during the last 3 years preceding this study. Sera were collected during allergen exposure (in the group with hymenoptera venom allergy not earlier than 4 months and not later than 6 months after a sting) and kept in temperature -70°C until tested.

Ethical approval was obtained for this study from the Ethics and Research Committee of the Silesian School of Medicine in Katowice. Informed consent was obtained from all subjects.

Methods. In all 4 groups there were evaluated: sCD23 serum level, total IgE serum concentration level of allergen-specific IgE against relevant allergens.

There were also assessed: clinical examination, skin prick test – blood donors were defined as atopic sub-

jects by the generally accepted criteria of PEPYS¹⁷. The skin prick tests were carried out at front of the forearm using a 1:1000 solution of histamine as a positive control, a 0.9% solution of NaCl, and a control solution delivered by the manufacturer as a negative control. The wheal diameter was estimated in millimetres and compared with the control and histamine reaction.

Immunological tests: sCD23 serum concentration was detected using sCD23 enzyme-linked immunosorbent assay kit from Binding Site (Birmingham, UK). This method serves for quantitation of the most stable product of autoproteolysis of CD23 with a molecular weight of 25 kDa. sCD23 concentrations for each well are calculated and printed out automatically. The sensitivity of this assay is $0.2\text{ }\mu\text{g/l}$. Allergen-specific IgE concentrations against perennial rye-grass, timothy-grass and June-grass in P group, against *Dermatophagoides pteronyssinus* in D group and *Hymenoptera venom* (*Apis mellifera*, *Vespidae*) in group I were estimated. Total and specific IgE serum concentrations against all allergens mentioned above were estimated by fluorometric method (FAST, Bio-Whittaker) according to manufacturer's instructions.

Statistics. The results were presented as median value, 25–75% range and total value range. Nonparametric tests (the U Mann-Whitney test and Kruskal-Wallis test) were used. Correlations were examined by the non-parametric Spearman's test. The level of significance was set at 0.05. Results were performed with a statistical package Statistica 4.1.

Results

sCD23 serum concentrations

Median value, 25–75% range and total value range in all investigated groups are shown in Fig. 1. Each group was subdivided with regard to total IgE serum level, higher than 250 U/ml and lower than 250 U/ml. These subgroups were named PP, DD, II (IgE>250 U/ml) and pp, dd, ii (IgE<250 U/ml). Median value, 25–75% range and total value range in investigated subgroups are shown in Fig. 2.

Patients with various allergic diseases expressed significantly higher concentrations of serum sCD23 comparing to healthy controls ($p<0.00005$, U Mann-Whitney test). No statistically significant differences were observed in sCD23 level among all groups of studied patients both in the subgroups of patients isolated with regard to the total IgE serum concentration ($p>0.05$, U Mann-Whitney test) as shown in Fig. 3.

Median value of total IgE serum concentration,

Table 1. Characteristic of the patients

Group	Number of patients	Sex		Age	
		male	female	range	mean value
P	18	8	10	20–45	30.7
D	25	12	13	16–50	29.9
I	12	3	9	16–55	36.6
K	18	8	10	17–34	25.9

P – group with pollen allergy suffering from seasonal allergic rhinitis.

D – group with house dust mite allergy suffering from perennial rhinitis.

I – group with hymenoptera venom allergy.

C – healthy controls without signs of atopy.

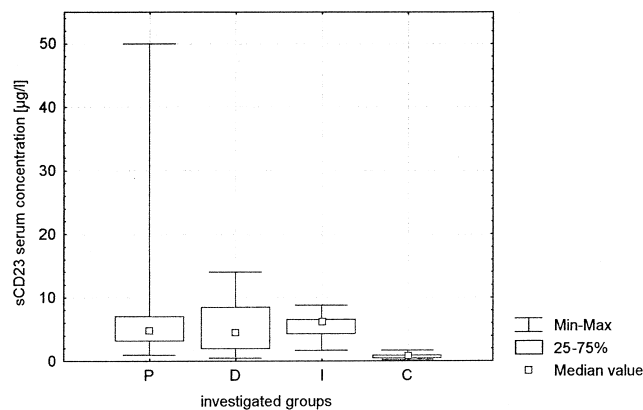


Fig. 1. sCD23 serum concentrations in investigated groups of patients (P – patients with pollinosis, D – patients with house dust mite allergy, I – patients with hymenoptera venom allergy, C – control group)

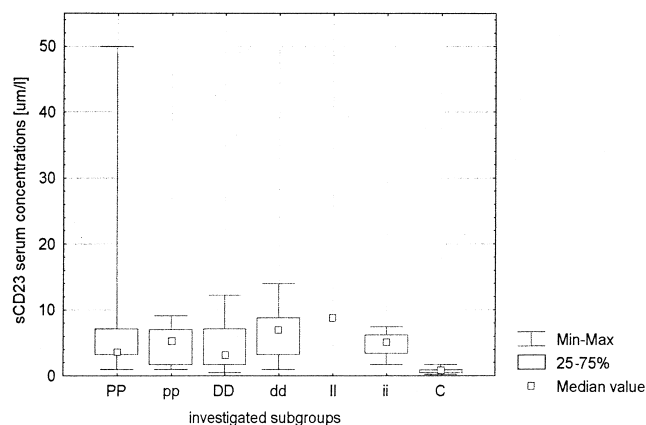


Fig. 2. sCD23 serum concentrations in investigated subgroups of patients with regard to the total IgE serum level ≤ 250 U/ml (pp – patients with pollinosis, dd – patients with house dust mite allergy, ii – patients with hymenoptera venom allergy) and with total IgE serum level > 250 U/ml (PP – subgroup with pollinosis, DD – subgroup with house dust mite allergy, II – subgroup with hymenoptera venom allergy), C – control group

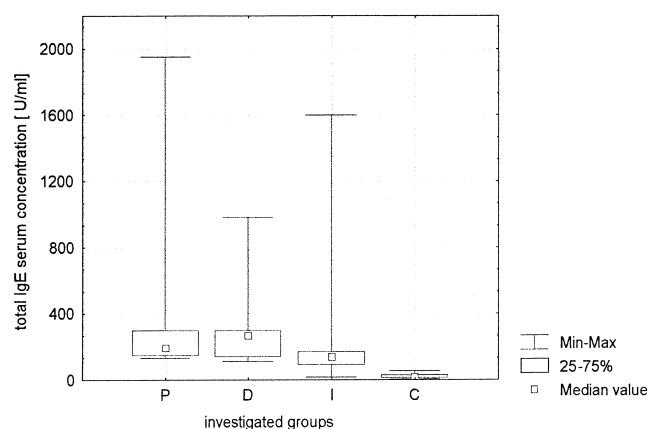


Fig. 3. Total IgE serum concentrations in investigated groups of patients (P – patients with pollinosis, D – house dust mite allergy, I – hymenoptera venom allergy, C – control group)

25–75% range and total value range in investigated groups are shown in Fig. 3. The total IgE serum levels were significantly higher in patients with various allergic diseases comparing to the control group ($p < 0.00005$, U Mann-Whitney test). Total IgE serum levels did not show any significant differences between studied groups P, D, I ($p > 0.05$, Kruskal-Wallis test).

Allergen-specific IgE concentrations against the relevant allergens were determined in all investigated groups. The level of clinical importance was from 1.00 to > 44.00 U/ml (class 1–6).

Correlations between sCD23 and total serum IgE concentrations

None of the investigated groups showed a statistically significant correlation between serum sCD23 level and serum total IgE concentration ($p > 0.05$, Spearman's correlation test; Table 2). In the groups of patients isolated from others with regard to the high level of total IgE there was no significant correlation between serum sCD23 level and total IgE as well ($p > 0.05$, Spearman's correlation test; Table 3). There were no statistically significant correlations between sCD23 serum level and allergen-specific IgE concentrations determined in all investigated groups ($p > 0.05$, Spearman's correlation test). None of the investigated groups showed a statistical significant correlation between

Table 2. Correlation between soluble CD23 and total IgE serum concentration in investigated groups

Group	r_s	p	n
P	0.18	0.49	18
D	–0.29	0.16	25
I	–0.26	0.41	12
K	0.19	0.44	18

r_s – Spearman coefficient of correlation.

p – significance level.

n – number of patients.

Further explanations see under Table 1.

Table 3. Correlation between soluble CD23 and total IgE serum concentration in investigated subgroups with total IgE serum concentration > 250 U/ml

Subgroup	r_s	p	n
PP	0.64	0.09	8
DD	0.11	0.69	15

PP – subgroup with pollinosis and total IgE serum concentration > 250 U/ml.

DD – subgroup with house dust mite allergy and total IgE serum concentration > 250 U/ml

Further explanations see under Table 2.

sCD23 serum concentration and the age of the patients ($p > 0.05$, Spearman's correlation test).

Discussion

The results of our study showed increased serum levels of sCD23 in 3 groups of allergic patients studied in comparison to healthy controls. Our criteria for selection of individuals for the study were in agreement with the generally accepted criteria for allergic diseases. Thus, the increased concentration of total and allergen-specific IgE in the majority of our patients was the expected result. As it has been mentioned above both CD23 cell surface molecule and its soluble form, sCD23 are considered to play a putative role in IgE-mediated immune response^{1, 3, 6, 8, 10}. SARFATI et al.¹⁹ proved that soluble CD23 may enhance IgE production via IgE-committed B cells. The CD23 cell expression and release of CD23 are controlled by IL-4, which plays a key role in IgE synthesis¹⁶. However, YAMAOKA et al.²¹ reported that IL-2, an activation marker of T cells, selectively enhances both CD23 expression on the surface of B cells and the autoprolysis of that molecule. The increase of membrane CD23 is also generated by prostaglandin (PGF₂), platelet activating factor (PAF) and leukotriene B₄ (LTB₄)¹⁸. Thus, the increased serum level of sCD23 in allergic patients, studied in our trial, may be related to the role of this molecule in the pathophysiology of altered immune response responsible for clinical manifestation of the underlying disease, despite the absence of correlation between sCD23 and IgE. sCD23 has been implicated in IgE regulation, but that is not the only role of this multifunctional receptor/cytokine. Membrane-bound CD23 appears to function as stimulatory molecule, whereas soluble form of CD23 can act as a factor of cell differentiation. Soluble CD23, estimated in our patients, would reflect the extent of the immune system dysregulation being the cause or the phenomenon associated with the clinical manifestation of the allergic disease.

Our results are consistent with the data of others who observed considerable increase of sCD23 serum level in patients with various types of allergic diseases including seasonal rhinitis, perennial rhinitis^{2, 4, 5, 9, 12, 14} and hymenoptera venom allergy and no correlations between sCD23 and IgE. However, none of them evaluated the sCD23 concentration with regard to the type of allergic disease. To our surprise the sCD23 serum level did not differ among the groups of our patients being allergic to different types of allergens and demonstrating different clinical picture of allergic disease.

The results deliver evidence that both the number of CD23⁺ peripheral blood cells and sCD23 level are considerably higher upon allergen exposure and/or IL-4 stimulation¹⁶. Similarly, SABBAAH et al.¹⁸ showed a statistically significant increase of the number of CD23 positive cells, sCD23, IL-2, IL-4, IL-6 and ECP (eosinophil cationic protein) levels parallel to the IgE serum concentration in atopic patients. It is worth to emphasise that although, in our trial, the sCD23 concentrations were estimated in serum of patients in asymptomatic period of the disease, these patients exhibited higher concentration of that molecule as compared with healthy donors. Although the role of sCD23 in normal physiological conditions is currently poorly understood, low quantities of sCD23 are detectable in serum of healthy individuals.

DELESPESSE and SARFATI⁷ showed a significant correlation between IgE and sCD23 serum concentrations in patients with bronchial asthma and allergic rhinitis. Searching for any relationship between evaluated variables we divided all patients included in the trial into two groups: those with IgE level > 250 U/ml and those with IgE < 250 U/ml. Even then no correlations between sCD23 and the IgE could be observed.

Taken together, we reasoned that sCD23 estimated in our patients could reflect the extent of the immune system dysregulation being the cause or the phenomenon associated with the clinical presentation of allergic disease. We conclude that: 1) sCD23 can be regarded as a useful, although non-specific marker of allergic disease; 2) sCD23 has no relevance to the type of allergic disease; 3) there is no correlation between sCD23 and IgE serum concentrations.

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