Are Allergen-Specific IgG Mainly IgG Anti-IgE Autoantibodies?

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Abstract

A large proportion of specific IgE occurred in immune complexes with anti-IgE autoantibodies in sera from nonhyposensitized allergic patients. These autoantibodies were misinterpreted as 'specific IgG' in different immunoassays such as dot immunoassays and the radioallergosorbent test (RAST), leading to overestimation of specific IgG. Purified immune complexes contained even more IgG than IgE antibodies. Heating of the complexes liberated specific IgE, producing an upwards RAST class shift. Thus anti-IgE autoantibodies are hiding the specific IgE, which is thereby underestimated. It is not known whether the hiding anti-IgE autoantibodies are also effectively neutralizing circulating or cell-bound IgE and might represent the actual blocking antibody.

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Results and Discussion

In a recent study we have observed an increase of specific IgG during hyposensitization therapy even in patients without therapeutical success [1]. On the other hand it is known that a large proportion of serum IgE occurs in complexes with IgG anti-IgE autoantibodies [2]. Thus, if specific IgE occurred in such immune complexes, we would not be able to distinguish whether measured IgG is directed against the allergen, or against allergen-specific IgE. We attempted, therefore, to purify specific IgE and IgG by affinity chromatography on allergen columns and further to separate specific IgE and specific IgG by affinity purification on a column coupled with monoclonal anti-IgE antibody (Le 27).

The serum pool, eluent and effluent fractions from the allergen affinity, as well as from anti-IgE affinity columns, were analyzed in a dot immunoassay. Unexpectedly, we found 'specific IgG' also in the sample eluted from the anti-IgE column. We detected indeed anti-IgE autoantibodies, which were predominantly present in immune complexes with IgE. These anti-IgE autoantibodies were capable of binding directly to IgE (PS) after purification. The amount of anti-IgE autoantibodies was very similar to the amounts of 'specific IgG' detected in the same assay. On the other hand, specific IgE was hardly detectable in the immuno-dot assay.

In immunoblotting, when using a monoclonal anti-IgG antibody (BS 17), again IgG was revealed in the eluent from the anti-IgE column, presumably representing IgG anti-IgE autoantibodies. In the effluent sample from the anti-IgE column, IgG was detected too, probably representing the real specific IgG. However, the monoclonal anti-IgE antibody BSW 17 failed again to detect IgE in the samples.

Therefore, we also used the commercial RAST assay (Pharmacia) for further analysis. In this immunoassay, in the sample eluted from the anti-IgE column, IgE was detected by polyclonal (Pharmacia) and by monoclonal anti-IgE (Le 27). Using anti-IgG BS 17 as developing antibody,

again 'specific IgG' was detected in the sample supposedly containing IgE only (anti-IgE eluent). When we heated aliquots of the samples for 30 min at 56 °C, more IgE became ac-

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cessible for determination using polyclonal and monoclonal anti-IgE antibodies. Thus, specific IgE was hidden by anti-IgE autoantibodies.

Our data indicate that anti-isotype autoantibodies should be considered as a major factor interfering with IgE determinations. IgE detection systems based on monoclonal antibodies were more affected by the presence of autoantibodies than such based on xeno-geneic antisera. Furthermore, so-called 'specific IgG' determined by different immunoassays may comprise a large proportion IgG anti-IgE autoantibodies. Thus, future studies will also have to analyze whether the rise of IgG during hyposensitization is due to an increase of the real specific IgG and whether autoantibodies are only hiding or also neutralizing ('blocking') circulating IgE.

References

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