

Editorial

Anti-cardiolipin antibodies in atopic dermatitis

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Atopic dermatitis (AD) is a common inflammatory skin disease with a complex, multifactorial etiology, probably caused by concerted actions of environmental and genetic factors (1, 2). An additional relevance of bacterial superantigens is discussed (3, 4). The disease is characterized by a number of immunological abnormalities. Cell-mediated immune hyperactivity, elevated IgE serum levels and the presence of eosinophil-derived mediators are well known features (5).

In this issue Szakos et al. (6) present a further immunological abnormality in AD patients. The authors report an association between the occurrence of anti-cardiolipin immunoglobulin (Ig)M and mite allergen-specific IgE antibodies in children with extrinsic type of AD. While detection of mite allergen-specific IgE is a typical feature of AD, anticardiolipin antibodies are reported especially in autoimmune diseases, e.g. in antiphospholipid syndrome (APS) or in patients suffering from systemic lupus erythematosus (SLE) (7). Szakos et al. hold mite proteins responsible for inducing specific anti-mite IgE and mite-lipids for provoking antibodies of the antiphospholipid-type antibodies, similar to the situation when lipids of microorganisms are initiating the production of anticardiolipin IgM during infections.

At first glance, this association between a typical feature of AD and a typical feature of systemic autoimmune disease astonishes, because clinical findings and genetic background of AD and autoimmune disorders are totally different. However, a few earlier studies revealed some common features between AD and SLE, a classical multiorgan autoimmune disease, e.g. elevated levels of antinuclear antibodies (8). Furthermore, both AD and SLE are mainly characterized by a predominance of Th2-type cytokines (while some Th1-type cytokines

[interleukin (IL)2, interferon γ] might play an additional role in inflammatory skin lesions). Both disorders present elevated levels of pathologic autoantibodies, in AD predominately allergen-specific antibodies of the IgE-type and in SLE predominately IgG- or IgM-type antibodies targeting nuclear proteins (5, 9).

Anti-cardiolipin antibodies (CLA) are reported in several clinical disorders including autoimmune, infectious and malignant diseases, as well as recently in AD (10). However, thrombosis and recurrent fetal loss associated with CLAs, constituting the APS are reported in autoimmune patients only, especially in patients suffering from SLE (7). β_2 -Glycoprotein (β_2 GPI) appears to be the major antigen for CLA. It is a highly conserved protein, with more than 80% homology between the amino sequences of human, bovine and rat counterparts (11). Therefore, nutritional contact of infant AD patients with β_2 GPI in milk and meat may lead to the generation of antibodies targeting the bovine as well as the human anti- β_2 GPI. A high frequency of IgG anti- β_2 GPI was found in patients with AD, but not in those with other allergic diseases. These anti- β_2 GPIs showed an epitope difference to the anti- β_2 GPI found in APS what may explain the nonthrombogenicity of these antibodies seen in children with AD (10).

The cause of specific antibody-production in AD and SLE is not yet clear. Probably, besides the contact with a corresponding antigen, additional immunoregulative factors are needed for their generation. In this context, especially an overexpression of Th2-type cytokines (e.g. IL4, IL5, IL0 and IL13) seems to be relevant.

The Th2 cytokines are not only undeniable factors of antibody-generation by B-cells, furthermore we know some examples of pathologically elevated antibody-

production driven by Th2 cytokines. It has been shown that virtually all children initiate IgG1 production against nutritional antigens at the age of 3 months, a time of Th2 predominance. This production typically peaks during infancy and wanes thereafter (12). High levels of IL 13 are associated with elevated mite-specific IgE levels (13).

It is well known that Th2 dominance in immune response is a general feature in newborns and during early infancy. Later on, children shift into Th1-predominance, but not those suffering from AD. Here Th2-predominance persists. The early pattern of Th2-dependent antibody production against nonpathogenic nutritional antigens fails to terminate in many children with AD, probably because in those young patients the immunological shift from Th2 to Th1 is disturbed (14, 15). Interestingly, in children suffering from diabetes mellitus type I, an autoimmune disease characterized by a Th1-type cytokine predominance, atopy symptoms have a

lower prevalence in comparison with age-matched control (16).

Co-emergence of autoimmune and allergen-specific antibodies in AD-patients underlines the wide variability of immune regulation in this disease. The association between specific anti-mite IgE and CLA demonstrates that specific patterns of immunological response are not limited to certain disorders. Predominance of Th2-type cytokine regulation in AD is one factor to explain this phenomenon, because similar features were also seen in other Th2-dominated disorders, but not in Th1-disease. However, an impact of other, possibly not yet identified factors cannot be excluded.

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