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Investigation of skin barrier functions and allergic sensitization in patients with Hyper-IgE syndrome

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Hyper-IgE syndrome (HIES) is a rare, but severe primary immunodeficiency, characterized by increased serum IgE levels as well as recurrent infections and atopic dermatitis (AD)-like skin lesions. Mutations in the STAT3 gene are detected in most of the HIES patients, which cause impaired Th17 development. AD is a common, chronic inflammatory skin disease with immunologic alterations (Th2-Th22 polarization) and characteristic skin barrier dysfunctions in the background. Our aim was to investigate the skin barrier alterations and allergic sensitization in HIES patients in order to compare it with those of AD patients and to find similar or different pathogenetic events in the development of skin lesions in these two diseases.

In our experiments STAT3 and filaggrin (FLG) mutation analyses were performed in HIES patients (n=6) and AD (n=30) patients served as controls. Laboratory parameters (LDH level and eosinophil count), immunologic alterations (intracellular cytokine staining), allergic sensitization (total and specific IgE levels, data from medical history), and skin barrier changes [transepidermal water loss (TEWL), serum thymic stromal lymphopoietin (TSLP) levels] were also examined.

Mutation analysis of STAT3 showed 100% positivity in HIES patients, although all of them had FLG wild-type genotype concerning the two most common mutations (R501X and 2282del4), which were found in 31% of our AD patients in heterozygous form. No differences were found between the two diseases regarding LDH and IgE levels or eosinophil counts. Impaired Th17 cell numbers were detected in T cells of HIES patients. No altered barrier functions were found in HIES patients, based on TEWL and serum TSLP levels, which were significantly impaired in AD patients. Allergic sensitization was detected more commonly in AD compared to HIES patients.

On the basis of these results barrier alterations probably are not the main pathogenetic events in the development of skin lesions in HIES. Despite of the high IgE levels, allergic sensitization is not a characteristic feature in these patients, which can be the consequence of their normal skin barrier functions, since outside-inside barrier impairment seems to be necessary for the development of allergic sensitization.