A Consistent Pattern of Minor Immunodeficiency and Subtle Enteropathy in Children With Multiple Food Allergy


Summary: Latcham et al. retrospectively studied 121 children with multiple food allergies collecting clinical, histologic and immunologic information in an attempt to find common patterns that might identify the child at risk. The children were divided into immediate hypersensitivity responders (group 1, n = 44) and delayed responders (group 2, n = 77).

The most common foods inducing immediate responses were milk, eggs and nuts. The most frequently recorded symptoms were urticaria, lip swelling and skin rash (86%). Delayed responses were also present in group 1. In fact, only three children (7%) had no delayed symptoms. The delayed responses in Group 1 were diet-responsive eczema, diarrhea, vomiting, wheezing and failure to thrive. The symptoms in group 2 were mainly eczema, failure to thrive and diarrhea and were induced most commonly by milk, soy, wheat, hydrolysates, eggs, meat and rice. Fourteen children in group 1 and 27 in group 2 had symptoms while exclusively breast fed. A family history of atopy was present in 90% of the children, particularly on the maternal side, as was a history of autoimmunity.

High immunoglobulin (Ig) E concentration, positive skin-prick tests and positive radioallergosorbent test were more frequent in group 1 than group 2 (50%, 70% and 75% vs. 18%, 27% and 25%, respectively). Both groups tended to have low-normal levels of IgA (45% of cases had IgA ≤0.3 g/L), skewing of IgG subclasses with increased IgG1 and decreased IgG2 and IgG3, and skewing of lymphocyte subsets with increased CD4 and CD19 and decreased CD8 and natural killer cells. There was also subtle evidence of enteropathy with focal lymphocyte or eosinophil infiltrate, villous blunting and reduced crypt/villus ratios.

Considering the difficulty in establishing a diagnosis of non-IgE-mediated food allergy, the authors propose that in a child with compatible symptoms, a family history of atopy or autoimmunity and the above described immunologic and histologic pattern might be helpful in supporting this diagnosis.

Comment: The prevalence of food allergy seems to be increasing in parallel with an increased prevalence of extrinsic asthma and environmental allergies. It is thought that these changes reflect changes in living conditions in western countries but also may reflect an increased awareness by medical person-
dence is compelling: allergies increase as material conditions improve.

Many studies indicate that there is a critical time early in infancy, possibly even during fetal life, when the genetically programmed atopic infant is at higher risk of becoming sensitized to food allergens. This might also be true with autoimmunity. This article raises the question of whether children with a strong family history of atopy and autoimmunity are also at increased risk of later autoimmunity. There are examples suggesting that this is indeed the case. Exposure to gluten before the age of 3 months in children genetically predisposed to diabetes type 1 (those with HLA DR3/DR4–DQ8 genotype, born of parents with type 1 diabetes) carries a fivefold higher risk for the development of islet autoantibodies (6). First exposure at the age of 7 months or older may also increase the risk for islet autoimmunity, possibly related to the larger amount of exposure at initial introduction (7). The timing of first exposure may influence immune tolerance to food antigens, and there may be an exposure time window that best allows tolerance to be achieved. Early introduction may lead to inflammation in the gut, altering the immune cell repertoire or leading to changes in islet β cells that may still be immature (6). MacFarlane et al. describe a wheat storage globulin protein, G1b1, that may be associated with islet cell damage. They also demonstrated that the sera from patients with type 1 diabetes has antibodies to G1b1, in contrast to sera from patients who do not have the disease (8).

Many questions remain unanswered and sometimes a new look at an old problem helps. Searching for other markers of allergy rather than the classic ones may be a productive line of investigation.

REFERENCES