

Circulating soluble L-selectin in atopic dermatitis

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Key words: atopic dermatitis; food allergy; oral provocation; soluble L-selectin.

• ALLERGIC reactions to food are the commonest manifestations of allergic diseases in infants and small children. In about one-third of children with atopic dermatitis, allergy to food components contributes to clinical symptoms. For diagnosis of food allergy, double-blind, placebo-controlled food challenges remain the cumbersome "gold standard". However, even in this

setting, merely clinical interpretation of skin reactions still may pose considerable difficulties, prompting efforts to look for suitable laboratory tools to monitor oral food challenges. Among these are eosinophil counts in peripheral blood, serum eosinophil cationic protein, tryptase, urinary N-methylhistamine, and various lymphocyte surface markers. So far, none of these parameters has significantly improved the diagnostic efficiency of double-blind, placebo-controlled food challenges.

The leukocyte surface transmembrane glycoprotein L-selectin (CD62L) plays a pivotal role in directing white blood cells into areas of acute and chronic inflammation, lymph nodes, and mucosal lymphatic tissue. After leukocyte activation both *in vitro* and *in vivo*, L-selectin is cleaved off the surface of human lymphocytes, neutrophils,

eosinophils, and other leukocytes within minutes. This generates soluble L-selectin (sCD62L), which can be found circulating in human plasma.

We have shown previously that lymphocytes isolated from children with atopic dermatitis undergo prolonged loss of L-selectin surface expression when stimulated *in vitro* with an allergen that provokes severe clinical symptoms *in vivo* (1). We also found loss of L-selectin expression in lymphocytes after antigen challenge *in vivo*, but not after placebo (2). While analysis of L-selectin surface expression by flow cytometry yields only relative data and requires immediate measurements due to the low stability of L-selectin surface expression, sCD62L concentrations can be quantitated exactly by enzyme-linked immunosorbent assay also in samples stored frozen at -20°C or -80°C for prolonged periods of time. We therefore now asked whether the immune activation causing the development of clinical symptoms in sensitized children after oral challenge with food allergens is associated with increased concentrations of circulating sCD62L.

Fifteen children aged 23 (12-41) months (median, range) diagnosed with atopic dermatitis, as defined by standardized diagnostic criteria (3, 4), were included in this study after informed parental consent. Dairy and egg products were excluded for at least 5 days from the children's food before antigen challenge.

Titration food challenges with hen's egg or cow's milk, respectively, were performed in a double-blind, placebo-controlled fashion, as described previously (5). Urticaria, wheezing, dyspnea, mucosal edema, nausea, and rapid deterioration of atopic dermatitis within the first 12 h after start of the food challenge were viewed as clinical reaction to the antigen.

sCD62L concentrations were determined by an enzyme-linked immunosorbent assay, as described previously (6), in plasma samples obtained from 15 children with atopic dermatitis before and 307 ± 166 min (mean $\pm$ SD) after starting oral challenges with the allergen. In 10 of these children, plasma samples were also obtained before and 363 ± 124 min after challenge with placebo ($P > 0.1$, paired *t*-test).

Circulating L-selectin (sCD62L) does not increase after oral food challenge of sensitized children.

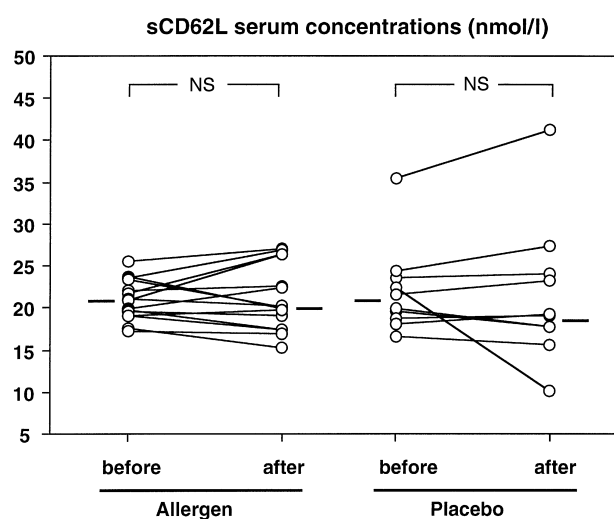


Figure 1. Positive reaction to patch tests with carbamazepine (in physiologic saline solution and in vaseline) after 48 h.

Clinical reactions to the suspected food allergen were observed in all 15 patients after hen's egg or cow's milk, respectively. Early-phase reactions (<2 h) were seen in 11 children, one child had a late-phase reaction only, and three children had both early-phase and late-phase reactions. An isolated or combined flare-up of atopic dermatitis was seen in eight patients. No patient experienced symptoms after placebo challenge. sCD62L serum concentrations were 20.9 ± 2.4 nmol/l before and 21.1 ± 3.9 nmol/l after starting allergen challenge ($P > 0.1$), and 22.0 ± 5.3 vs 21.5 ± 8.4 nmol/l before and after placebo, respectively ($P > 0.1$) (Fig. 1).

The frequency of effector leukocytes that are involved in an allergic reaction and undergo L-selectin cleavage may be too low to detect L-selectin shedding by quantitating shed sCD62L. The number of sCD62L molecules in whole blood exceeds that of surface-expressed L-selectin molecules; therefore, activation-induced L-selectin shedding of more than 10% of circulating leukocytes may be required during a generalized reaction to get a significant increase of sCD62L plasma concentrations, although sCD62L generated in compartments other than the blood may also contribute to sCD62L plasma concentrations. In neonates with acute bacterial infection, loss of L-selectin lymphocyte surface expression (7) is not accompanied by an increase of plasma sCD62L concentrations (6). In addition, acute inflammation may also lead to enhanced vascular sequestration of sCD62L (8), thereby counteracting the effect of increased rates of proteolytic release of sCD62L.

Acute reactions to food allergens in sensitized subjects may be subtle, dramatic, or even life-threatening, but laboratory changes persistently accompanying these reactions have not been identified so far. While the release of sCD62L reflects leukocyte activation, which is a hallmark of allergic reactions, this study failed to demonstrate a significant change of sCD62L serum concentrations in response to food allergens

that provoke clinical reactions in sensitized children with atopic dermatitis. We conclude that measuring sCD62L concentrations in serum does not appear to be useful in monitoring oral food challenges in children with atopic dermatitis.

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Anticonvulsant hypersensitivity syndrome due to carbamazepine

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Key words: carbamazepine; drug hypersensitivity; drug-hypersensitivity diagnosis.

● ANTICONVULSANT hypersensitivity syndrome (AHS) is an uncommon adverse effect of exposure to phenytoin, carbamazepine, or phenobarbital (1). We describe a case of AHS induced by carbamazepine where the diagnosis was established by patch test.

A 20-year-old man arrived at our hospital with an infectious, mononucleosis-like syndrome. Three weeks before, the patient had started therapy with risperidone, carbamazepine, citalopram, and adenometionine for a depressive syndrome. Mild pruritus and furunculosis on his head were the first symptoms. Subsequently, lymphadenopathy involving the cervical chain appeared and also a fever (maximum 38.5°C) that was treated with nimesulide, ketoprofen, and noramidopiridine. A macular eruption began on the face and moved down the body. Scarlet fever was suspected, and the patient started therapy with amoxicillin plus clavulanic acid associated with acetylsalicylic acid. The maculopapular eruption worsened, and angioneurotic edema appeared on one eye. The patient was then hospitalized. Routine laboratory studies showed hypereosinophilia (14%=980/μl); monocytosis (16%=1300/μl); elevation in serum transaminase (SGOT=253, SGPT=622), alkaline phosphatase (375 UI/l; normal=50-300), and γGT (131 UI/l; normal=10-50); and hyperuricemia of 9.2 mg/dl (normal=2.5-7). Serology for EBV, *Toxoplasma gondii*, rubella virus, CMV, HIV,

Positive patch tests suggested a cell-mediated allergic response.