News Release

Title; Antigen-specific IgG4 increase in atopic dermatitis with long-term dupilumab use

Key Points

- Atopic Dermatitis
- antigen-specific IgG4
- dupilumab

Summary

Our prospective study investigated the changes in antigen-specific IgG4 (sIgG4) that occur during long-term dupilumab treatment in patients with atopic dermatitis. IgG4 is an antigen-neutralizing antibody that is known to have anti-allergic effects because it competes for the binding site of IgE. While dupilumab has been reported to have an inhibitory effect on B cell maturation, the increase in sIgG4 during dupilumab treatment may indicate that dupilumab indirectly improves allergies in those predisposed to them. We present the possibility of a new therapeutic effect of long-term dupilumab use.

Research Background

Atopic dermatitis (AD) is a chronic, non-infectious inflammatory dermatosis with multiple causative factors, such as skin barrier dysfunction, microbial imbalance, immune dysregulation, and environmental triggers. Dupilumab, an interleukin-4 receptor a (IL-4Ra) antagonist, has been widely used as a biologic to treat severe AD. Dupilumab blocks the type 2 (TH2) differentiation and activation of T helper cells and affects both T cells and B cells. Blocking IL-4Ra signaling affects B cell maturation, germinal center formation, B–T cell interaction, and adequate antibody class switching for IgE production. Furthermore, IL-4Ra knockout AD mice show lower rates of IgG-positive B cells to total B cells than control AD mice show.

Allergen-specific IgG4 (sIgG4) is known to increase during allergen-specific immunotherapy, and sIgG4 production levels strongly correlate with allergen-specific tolerance4. sIgG4 has the ability to inhibit B cell and basophil activation by competitively binding to the allergen-specific IgE (sIgE) binding sites.

Research Results

We established an allergen-specific ELISA to measure sIgE and sIgG4 for Dermatophagoides farinae (house dust mite), Cryptomeria japonica (Japanese

cedar) pollen, Canis familiaris (dog) skin, and Candida albicans. Total serum IgE and sIgE for house dust mites was significantly decreased after dupilumab treatment and sIgG4 for house dust mites was significantly increased ($p<0.05$), despite decreased levels of serum total IgG4 ($p<0.05$), but there were no significant changes in sIgE or sIgG4 for house dust mites in the topical treatment group ($p=0.87$ and $p=0.14$, respectively). the sIgG4/sIgE ratio was compared before versus after treatment, the sIgG4/sIgE ratios were found to be higher for all antigens after treatment with dupilumab than after topical treatments only.

Research Summary and Future Perspective

Our results may indicate a new indirect anti-allergic effect of dupilumab via the upregulation of sIgG4 production.

Publication

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