Differentiation between control subjects and patients with chronic spontaneous urticaria based on the ability of anti-IgE autoantibodies (AABs) to induce FcεRI crosslinking, as compared to anti- FcεRIα AABs

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Introduction: Chronic spontaneous urticaria (CSU) is defined as the occurrence of systemic daily wheals for at least 6 weeks. Since the presence of IgG autoantibodies (AABs) to FcεRI α-chain (FcεRIα) and IgE has been repeatedly observed in patients with CSU, autoimmunity is thought to be one of the major causes of CSU. The reported prevalences of IgG autoantibodies to FcεRIα and IgE in sera from patients with CSU have varied, and these AABs are also often observed in healthy control subjects. Regarding the histamine release activity of purified IgG from patients with CSU, the number of examined patients has been small.

Objective: We sought to determine the prevalence and FcεRI crosslinking ability of these AABs in a large number of patients with CSU and nonatopic control (NC) subjects.

Methods: We compared the concentrations of anti-IgE and anti-FcεRIα AABs and the ability of these AABs to cause FcεRI aggregation in patients with CSU (n = 134) and NC subjects (n = 55) using ELISA and an *in vitro* elicitation test, respectively.

EXiLE (IgE crosslinking-induced luciferase expression) test:

The luciferase-reporting mast cell line (RS-ATL8) which expresses human FcεRI was used to measure mast cell activation by anti-FcεRIα and anti-IgE AABs from patients with CSU. The luciferase expression levels were represented as the fold increase in light units compared with the results in non-stimulated cells. (Figure 1)

Result 1: The concentration of anti-IgE AABs was significantly different between the NC subjects and the CSU patients ($P < 0.0001$, cutoff value: $0.558 \mu\text{g/mL}$), whereas the concentration of anti-FcεRIα AABs was not. Significant correlation was not seen between the concentrations of anti-FcεRIα and anti-IgE AABs in both NC subjects and patients with CSU (data not shown).

(Figure 2) Abbreviations: OR, Odds ratios

Result 2: The ability of anti-IgE AABs, but not anti-FcεRIα AABs, to induce FcεRI crosslinking was significantly higher in CSU patients than in NC subjects ($P = 0.0106$). Significant correlation was not seen between the concentrations of anti-IgE AABs and the levels of FcεRI crosslinking in NC subjects and CSU patients (data not shown). (Figure 3)

Discussion: In the Japanese population of CSU patients studied, the ability of the anti-IgE AABs to induce FcεRI crosslinking differed significantly between NC subjects and CSU patients, suggesting the involvement of anti-IgE AABs in the pathogenesis of CSU in the Japanese population.

Figure 2

Figure 3