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Atopic status and thyroid autoimmunity do not predict omalizumab response in severe chronic spontaneous urticaria patients

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Key words

Urticaria; thyroid autoimmunity; atopic status; total IgE; omalizumab.

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To the Editor,

chronic spontaneous urticaria (CSU) is a rather frequent disease of variable severity characterized by recurrent wheals with or without angioedema for more than 6 weeks. Some patients show a continuous and very severe disease refractory to antihistamine treatment which worsens dramatically their quality of life. The anti-IgE mAb omalizumab is indicated as second line treatment in these cases. The clinical response largely depends on the endotype (either IgG-mediated autoimmune [type IIb] or IgE-mediated "autoallergic" [type I]) of the disease. Positive *in vitro* tests of basophil activation (either BAT or BHRA), antinuclear antibodies, autologous serum skin test (ASST) and low total IgE levels have been associated with a slow or absent response to the drug (1-5). Conversely, elevated total IgE are generally associated with a prompt response to omalizumab (5-12). Atopic diseases are a well-known cause of elevated IgE, but whether atopic status may be used as a marker of Type I CSU, thus predicting a rapid response to omalizumab, is still unclear (11). The association between CSU and thyroid autoimmunity has been known for almost 30 years (12), but, although typical type IIb CSU patients frequently show low IgE and autoimmune thyroiditis (14), whether thyroid autoimmunity may alone predict a poor or absent response to omalizumab is still undefined. In one study, the prevalence of thyroid autoimmunity was similar in CSU patients with different levels of total IgE (15). The present study investigated whether atopic status and thyroid autoimmunity may be practically useful to discriminate type I and type IIb CSU.

Total IgE levels and thyroid autoantibodies were measured, and atopic status was ascertained by SPT with airborne allergens before omalizumab treatment in 260 consecutive patients with severe CSU (M/F 88/172; mean age 49.5; mean disease duration 50.5 months (range 2-720 month), baseline UAS-7 level > 28). Based on the clinical response, patients were divided into early- (ER), late- (LR), and non- (NR) responders to omalizumab. An early response was defined as a reduction of at least 50% of the UAS-7 score within 4 weeks after the first administration. A late response was diagnosed if a reduction > 50% of UAS-7 score occurred 1-3 months after the start

of the drug. Non-response was defined as the absence of any significant change in UAS-7 3 months after the start of the treatment. The chi-square test with Yates' correction, the two-tailed Student's t-test, or the Mann-Whitney non-parametric test were employed to compare the study groups where appropriate. Probability values < 5% were considered statistically significant. The internal review board of the clinic approved this retrospective, anonymous study.

79/260 (30%) of patients were atopic and 60/238 (25%) showed thyroid autoimmunity. On omalizumab treatment, 160 (61%) were ER, 55 (22%) LR, and 45 (17%) NR. In these 3 subgroups, 55 (34%), 15 (27%), and 9 (20%) patients, respectively, were atopic (p = NS), and 36/149 (24%), 14/49 (29%), and 10/40 (25%), respectively, showed signs of thyroid autoimmunity (p = NS). The median total IgE levels in the 3 subgroups were 154 IU/ml, 51 IU/ml, and 20 IU/ml, respectively (p < 0.05 for ER *vs* LR + NR; p < 0.05 for ER *vs* NR; p = NS for LR *vs* NR) (**figure 1**). Total IgE levels < 20 IU/ml were found in 11%, 19%, and 50% of patients, respectively (p < 0.001 for ER *vs* NR). Total IgE levels > 100 IU/ml were detected in 60%, 38%, and 21% of patients, respectively (p < 0.001 for ER *vs* NR; p < 0.005 for ER *vs* LR; p = NS for LR *vs* NR) (**figure 2**). 9/48 patients with thyroid autoimmunity showed total IgE levels < 20 IU/ml; such association was observed in 4/27 ER (15%), 1/13 LR (8%), and 4/8 NR (50%) (p < 0.05 for NR *vs* ER + LR).

This study confirmed the high prognostic value of baseline total IgE levels for omalizumab response (5-12). In contrast, it showed that atopic status cannot be adopted as a marker of Type I CSU or as a predictor of omalizumab response in CSU patients. Similarly, although confirming the well-known association between CSU and thyroid autoimmunity, the study shows that thyroid autoimmunity *per se* cannot be considered as a marker of Type IIb CSU or a predictive marker of poor response to omalizumab (15). Altogether, the detection of type IIb CSU patients requires the concordance of a series of different tests, including the autologous serum skin test, *in vitro* basophil activation tests, and positive IgG anti-FcεRI or anti-IgE (3). In conclusion, total IgE levels currently remain the only and most easily available prognostic marker for omalizumab response in patients with severe CSU.

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None.

Contributions

RA entirely contributed to this work.

Conflict of interests

The author declare that he has no conflict of interests.

Figure 1 *- Median IgE levels in the 3 subsets of omalizumab responders.*

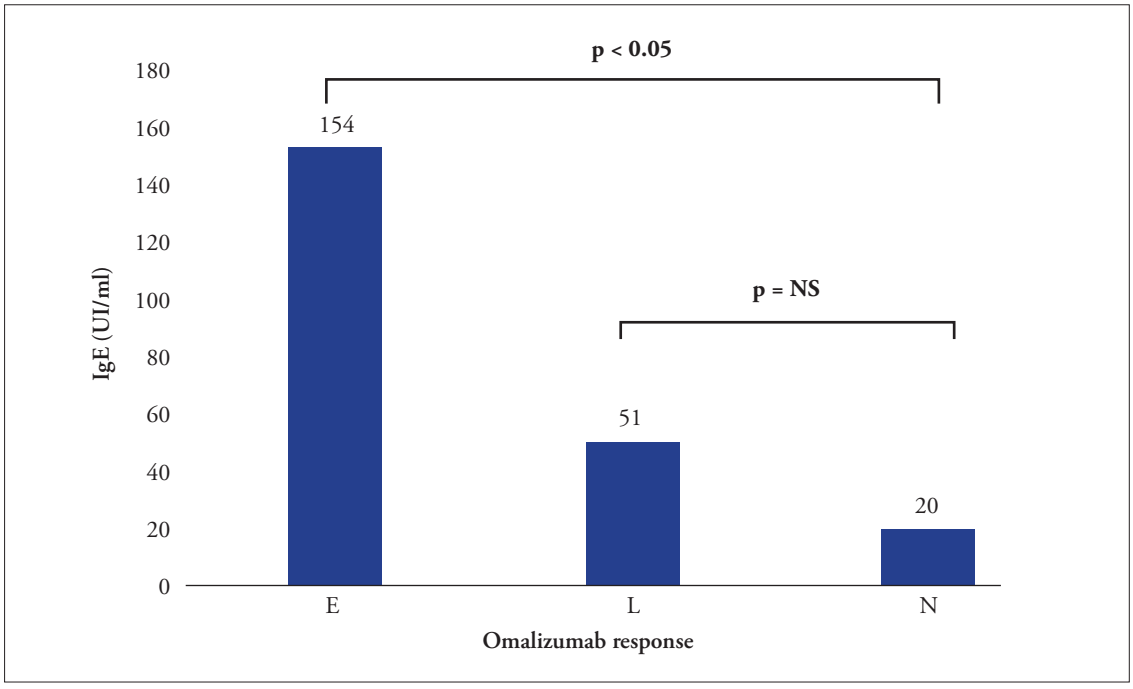
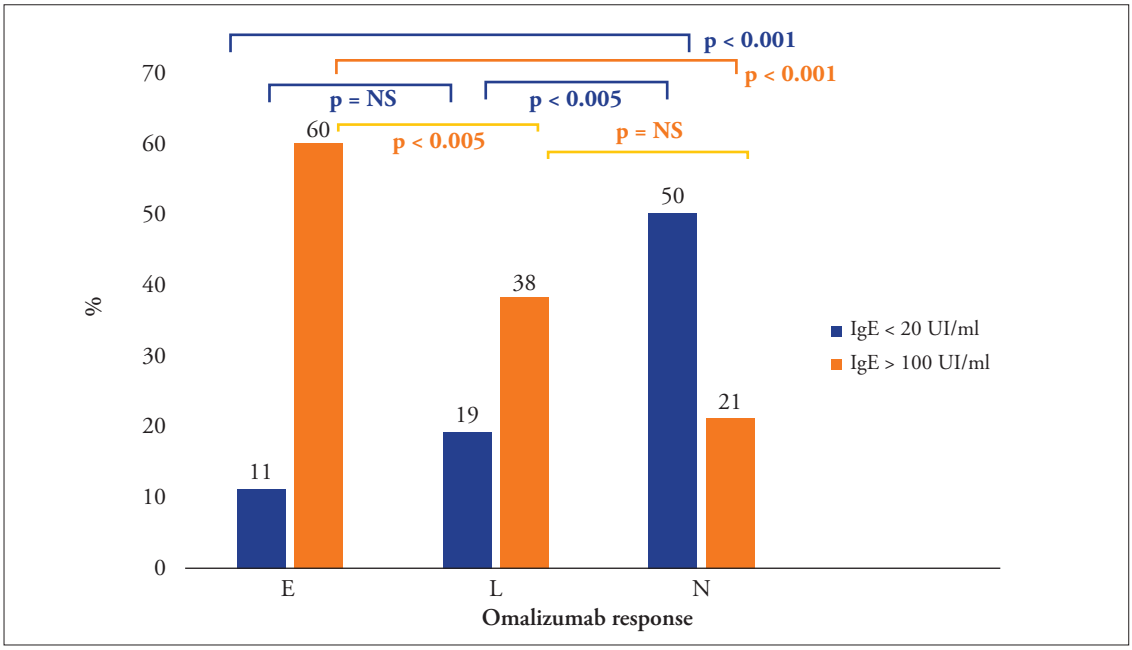


Figure 2 *- Prevalence of low (< 20 IU/ml) and high (>100 IU/ml) levels of total IgE in the 3 subsets of omalizumab responders.*



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