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Letters

Addition of omalizumab to antihistamine treatment in chronic urticaria

A real-world study in China

Chronic urticaria (CU) is a common skin disorder that is characterized by the occurrence of wheals, angioedema, or both for more than 6 weeks. It is further divided into chronic spontaneous urticaria (CSU) and chronic inducible urticaria (CIndU).[1] To date, the humanized anti-immunoglobulin E monoclonal antibody omalizumab has become well recognized as an effective and well-tolerated therapy for patients with CU who remain symptomatic while taking H_1-antihistamines. However, no data are available from China; therefore, this study was designed to describe omalizumab treatment patterns since the agent became available in China to better understand its treatment outcomes, potential predictors for treatment efficacy, and relapse and retreatment in a real-world setting.

To this end, we performed a retrospective, single-center, investigator-initiated observational study at our Urticaria Center of Reference and Excellence between February 2018 and October 2019.[2] The study was approved by the China Ethics Committee of Registering Clinical Trials. The study was designed and implemented in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki.

We included 89 antihistamine-resistant patients with CU, among whom 66 had CSU, 16 had CIndU, and 7 had both CSU and CIndU. Our patients were predominantly female (59 [66.3%]) and had a mean (SD) age of 37.45 (16.32) years. The omalizumab treatment period was 6 months (interquartile range [IQR], 4-10 months). All patients had a baseline urticaria control test (UCT) score of less than 12 despite taking H_1-antihistamines, which indicated an uncontrolled disease status.

The UCT was used to assess treatment efficacy for all patients in our study. The minimum and maximum UCT scores were 0 and 16, respectively, with low points indicating high disease activity and poor disease control.[1] A complete response was defined as a UCT score of 16, partial response as a score of 12 to 15, and nonresponse as a UCT score less than 12 or the requirement for additional use of immunosuppressive agents or corticosteroids to control symptoms during the treatment periods.[1] Patient quality of life was assessed by the Dermatology Life Quality Index (DLQI), where higher scores indicated poorer quality of life. The Urticaria Activity Score summed over 7 days (the international guideline—recommended once-daily version) was also applied to assess the disease activity for those who had CSU.[1] Relapse was defined as the reappearance of CU symptoms (UCT score <12) in complete responders after discontinuation of omalizumab treatment.

Of the 89 patients, 67 (75.3%) attained complete response and 13 (14.6%) achieved partial response, whereas 9 (10.1%) did not respond to omalizumab. The UCT score significantly increased from 3.0 (IQR, 1.0-6.0) to 12.0 (IQR, 4.5-14.0) as early as the first month ($P < .001$) and continued to improve and maintained a high level during the study period (Fig 1A). The DLQI score significantly decreased from 16.0 (IQR, 12.0-20.5) to 7.0 (IQR, 1.0-13.5) as early as the first month ($P < .001$) and kept decreasing and remained low during the study period (Fig 1A). In addition, 58 of the 73 patients (79.5%) who had CSU could achieve a Urticaria Activity Score summed over 7 days score of 6 or lower, which indicated a minimal disease activity.

Nonresponders had lower baseline total immunoglobulin E (IgE) levels (17.0 vs 98.0 kU/L, $P = .003$), longer disease durations (72.0 vs 24.0 months, $P = .04$), and shorter treatment periods (5.0 vs 8.5 months, $P < .001$) compared with responders. The response rates showed no major differences among patients with and without angioedema (85.7% vs 92.6%, $P = .49$).

We tried to discontinue omalizumab treatment in 31 patients with CU with complete response, and 21 (67.7%) of them experienced a relapse despite continued antihistamine treatment within 3 to 16 weeks after their last omalizumab injections (Fig 1B). The other 10 patients had sustained well-controlled status for a minimum of 8 weeks and a maximum of 12 months after their last omalizumab injections. Patients with disease relapse had higher baseline total IgE levels (150.0 vs 72.5 kU/L, $P = .01$) and longer disease durations (84.0 vs 18.0 months, $P = .001$) than patients without disease relapse. Age, sex, positivity for autologous serum skin test or thyroid autoantibodies, or types of urticaria did not markedly differ among patients with and without disease relapse. A total of 9 patients with disease relapse reinitiated omalizumab treatment. All reported a rapid and marked response after the first injection of retreatment.

This was the first report, to the best of our knowledge, on the use of omalizumab for the management of CU in China. We found that omalizumab provides rapid and effective symptom relief in Chinese patients with CU. More than three-quarters of the patients gained complete response, and an additional 14.6% of the patients achieved partial response. These numbers were very much in accordance with other real-life studies.[3] The reported complete response rates in the real-world clinical settings ranged from 70% to 82%, and the reported partial response rates ranged from 10% to 22%.[3] Omalizumab treatment also markedly improved patient quality of life as assessed by the DLQI. Low levels of quality of life impairment were maintained throughout the treatment period.

Our study found that nonresponders tend to have lower baseline total IgE levels, confirming the findings of previous studies.[4,5]

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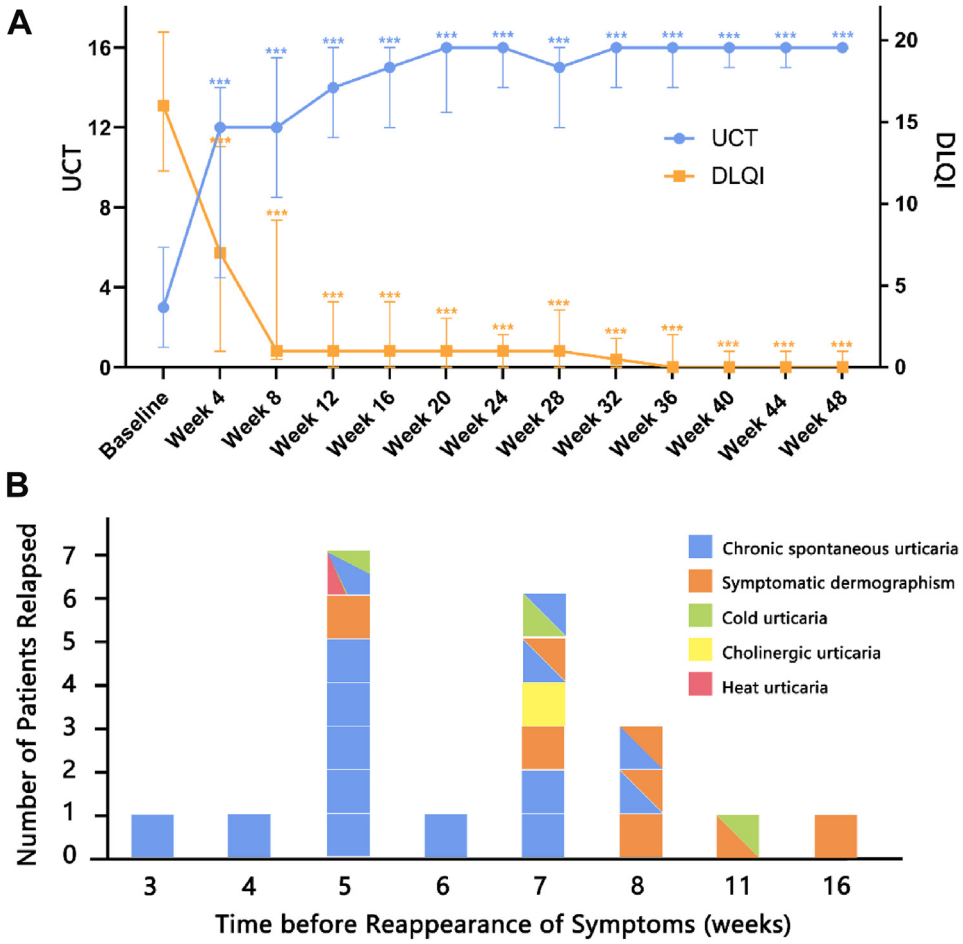


Figure 1. (A) Variations in urticaria control test (UCT) and Dermatology Life Quality Index (DLQI) scores. (B) Time to relapse after omalizumab treatment discontinuation. DLQI, Dermatology Life Quality Index; UCT, urticaria control test. *$P < .005$.

This finding may be attributable to autoimmunity in which IgG autoantibodies might play a more crucial role.[4] Autoimmunity is linked to delayed response; therefore, some of the nonresponders are likely to respond if they continued their omalizumab therapy. The fact that responders tend to have longer treatment periods in this study supported this notion. In addition, non–IgE-mediated activation pathways might also be involved in some of the nonresponders.[6]

Moreover, omalizumab is a symptomatic treatment, and symptoms almost invariably reoccur when treatment is stopped. In clinical trials and in real-life clinical settings, relapse rates ranged from 17.6% to 67%.[7] We confirmed these findings and noted a interval of 3 to 16 weeks until symptoms began to reoccur for most patients. We found that patients with relapse had longer disease durations and higher total IgE levels than that of patients without relapse. Furthermore, all patients who reinitiated omalizumab treatment experienced a rapid and substantial response, supporting omalizumab retreatment as an effective option for patients who had previously benefited from initial omalizumab treatment.

Potential limitations of the study were its noninterventional design and the likelihood of patient loss to follow-up. The efficacy of omalizumab for angioedema was not systematically studied using an angioedema activity score or an angioedema quality-of-life questionnaire in this study.

The findings of this study are useful for not only physicians in China but also individuals worldwide who adhere to the international guideline. Patients experienced substantial improvements of symptoms immediately after 1 month of omalizumab treatment and continued to benefit throughout the entire treatment periods. Patients with higher baseline total IgE levels and longer disease durations are more likely to experience relapse after discontinuation of omalizumab treatment. However, retreatment was also rapidly acting and highly effective.

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