

Use of omalizumab in uncontrolled chronic spontaneous urticaria also improved latex-induced contact urticaria



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Clinical Implications

- Contact urticaria is characterized by wheals and angioedema that occur in response to contact with urticariaogenic substances (eg, latex). This is the first report that shows the beneficial effect of omalizumab in a patient with contact urticaria.

TO THE EDITOR:

Chronic urticaria (CU) is divided in 2 subtypes: chronic spontaneous urticaria (CSU) and chronic inducible urticaria, of which there are several subtypes.¹

The efficacy and safety of subcutaneous omalizumab for the treatment of CU has been established in several randomized placebo-controlled trials and confirmed in real-world clinical studies.² Suitable treatment options are still lacking for patients with severe disabling H1 antagonist-resistant inducible urticaria.

Here, we report the effects of omalizumab in a patient with CSU along with latex contact urticaria.

Our patient, a 48-year-old white nurse, who had uncontrolled CSU since 2011 and was treated with antihistamines long-term therapy up to 3 times the standard dose (loratadine, desloratadine, ebastine, rupatadine) and short-term glucocorticoid treatments (during exacerbations) without benefit. During the last 2 years, she complained of itching and hives after wearing latex gloves without powder.

Routine blood investigations, abdominal ultrasound, and chest and paranasal sinuses radiography were carried out with negative results (Table I).

To diagnose latex contact allergy, serum-specific IgE to natural rubber latex (NRL) (positive if >0.10 kUA/L) (Table I), serum-specific IgE to recombinant allergens for *Hevea brasiliensis* (rHev b 1, 3, 5, 6.01, 6.02, 8, 9, and 11) dosed by ImmunoCap System (ThermoFisher, Uppsala, Sweden), and skin prick tests (SPTs) both with commercial extract (Alk-Abello, Milan, Italy) and with glove extract prepared, as previously reported,^{3,4} were performed. Additional SPTs were performed with foods and common inhalant allergens (Lofarma, Milan, Italy). A glove use test was performed with the same gloves (same lot) used for SPTs as previously reported.^{3,4} Symptoms were scored 1 for local itching without any other manifestations, 2 for redness, 3 when wheals became apparent, and 4 if any systemic reaction appeared. SPTs with commercial and extemporaneous extracts with latex were positive (Table I), whereas SPTs with food and common inhalant allergens were negative. Glove use test gave the positive result with the

appearance of erythema, wheals, and pruritus 20 minutes after wearing (score 3) (Figure 1). In addition, we found positive results to serum-specific IgE to NRL and to rHev b 1 (Table I) confirming the latex contact urticaria diagnosis.

We evaluated the lack of response to previous therapies in CSU, and we chose to administer omalizumab (300 mg every 4 weeks for 24 weeks) as an add-on therapy to second-generation H1 antihistamines according to the Italian Medicine Agency (AIFA) for CSU.⁵ CSU disease activity in the patient was determined by Urticaria Activity Score 7 (UAS7), which was 29 before anti-IgE treatment, despite a stable dose of H1 antihistamine (Table I).

The patient reported complete remission of CSU within 2 weeks after the first injection and continued to receive 300 mg of omalizumab every month for a total of 24 weeks, without experiencing any symptoms (UAS7 = 0). In addition, during the omalizumab treatment, at week 16, the patient told us that she had occasionally come into contact with latex gloves without symptoms. We decided to perform latex skin and glove use tests again 24 weeks after the first injection of omalizumab. IgE test showed a partial decrease in sensitization (the SPT positive reaction to latex extract dropped from 1:100 to 1:10, the SPT to commercial latex extract declined in mean diameter from 6.7 to 4.2 mm, the serum-specific IgE to latex from 8.9 to 8.3 kUA/L and to rHev b 1 from 6.8 to 6.7 kUA/L). A longer exposure to the glove was needed to provoke a reaction (approximately 80 minutes) with a score 2.

In reality, because of the hypothesized different mechanisms of action of omalizumab (it lowers IgE levels and downregulates IgE receptors, reduces mast cell releasability, reduces activity of IgG autoantibodies against FcεRI and IgE, reduces activity of intrinsically “abnormal” IgE, and reduces activity of IgE autoantibodies against an autoantigen),⁶ its fields of application are widespread even though its use is still off-label for many diseases such as anaphylaxis, keratoconjunctivitis, drug allergy, nonatopic asthma, atopic dermatitis, nasal polyps, Churg-Strauss syndrome, eosinophilic otitis media, chronic rhinosinusitis, bullous pemphigoid, and contact dermatitis.⁷

Contact urticaria is an inducible form of urticaria and it is defined by the development of urticaria lesions within minutes after contact to an exogenous agent (eg, latex).¹ To our knowledge, this case represents the first report that shows the beneficial effect of omalizumab in a patient with contact urticaria.⁸

In our case, it is possible to hypothesize that the reduction of latex skin sensitization in association with a decrease of grade of latex positivity on IgE tests is due to the omalizumab mechanism that binds the Fc3 subunit of free IgE molecules. So, the reduced binding of free specific IgE to the high-affinity IgE receptor (FcεRI) leads to a reduced density of specific IgE on the surface of mast cells and basophils, and to the downregulation of the receptor itself.⁹ As is already demonstrated, also in our patient omalizumab might have induced the depletion of FcεRI in skin mast cells leading to a favorable response in latex contact urticaria.¹⁰ Further studies are needed to confirm our results in a larger sample of patients and to evaluate the persistence of latex tolerability after discontinuation of omalizumab.

TABLE I. Patient's demographic and baseline characteristics

Parameters	Details
Age	48 y
Sex	Female
Weight	73 kg
Race	White
Time since diagnosis of CSU	7 y
In clinic UAS*	5
UAS 7†	29
Weekly ISS†	16
Presence of angioedema	No
Tests with normal results	CBC with differential; ERS; CRP; stools analysis for parasites; urinalysis; hepatic and renal functions; hepatitis B and C serologies; antinuclear antibody; TSH; antiperoxidase antibody; antimicrosomal antibody; antithyroglobulin antibody; serum protein electrophoresis; anti-toxoplasma antibody; anti-Helicobacter pylori antibody; C3, C4 complements; abdominal ultrasound; chest and paranasal sinuses radiography
ASST	Negative
Total IgE level	193.8 kU/L (normal value < 100 kU/L)
Serum-specific IgE to NRL	
NRL	8.9 kUA/L
rHev b 1	6.8 kUA/L
Latex SPT (commercial extract)	Positive (mean wheal diameter 6.7 mm)
Latex SPT (extemporaneous extract)	Positive (dilution 1:100)
Latex glove use test	Positive (pruritus, erythema, and wheals) at 20 min

ASST, Autologous serum skin test; CBC, complete blood count; CRP, C-reactive protein; CSU, chronic spontaneous urticaria; ESR, erythrocyte sedimentation rate; ISS, itch severity score; NRL, natural rubber latex; SPT, skin prick test; TSH, thyroid stimulating hormone; UAS, urticaria activity score.

*Defined as the highest value from the day 14 visit, day 7 visit, and day 1 visit.

†Based on data collected in the patient daily diary in the 7 days before the first treatment date.

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FIGURE 1. Glove use test: positive result with the appearance of erythema, wheals, and pruritus 20 minutes after wearing (score 3).

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