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Antihistamine-resistant urticaria factitia successfully treated with anti-immunoglobulin E therapy

K. Krause, E. Ardelean, B. Keßler, M. Magerl, M. Metz, F. Siebenhaar, K. Weller, M. Worm, T. Zuberbier, M. Maurer*

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Urticaria factitia (also known as dermographic urticaria and symptomatic dermographism) is characterized by whealing and itching following a minor stroking pressure, rubbing or scratching of the skin. The majority of patients with urticaria factitia benefits from treatment with nonsedating antihistamines. Some patients, however, do not achieve adequate symptom control even with updosing of antihistamines (1) and may suffer from substantial quality of life impairment (2).

A possible new treatment alternative and insight into the pathogenesis of urticaria factitia.

We present the case of a 48-year-old Caucasian woman with a 3-year history of severe urticaria factitia. Minimal shear forces to the skin produced massive pruritus and whealing, and basic daily activities such as getting dressed or combing her hair provoked intense symptoms. Furthermore, the patient complained of a disturbed work performance and general reduction in mental and physical fitness. Having been treated with various nonsedating antihistamines in standard and higher than standard doses, the patient eventually received a combination of an antihistamine four times the standard dose (ebastine), an H2 blocker (ranitidine) and a leukotriene antagonist (montelukast). However, none of these treatments resulted in sufficient symptom control and the patient remained severely affected in her every day life.

Dermographometer skin testing with 36 g/mm^2 demonstrated marked whealing and pruritus (Fig. 1). The patient was otherwise healthy based on the results of our diagnostic workup, which did not show pathological results with the exception of elevated total IgE (341 kU/l).

In August 2009, after obtaining permission from the patient's health insurance, we started her on anti-IgE (omalizumab, Xolair®, Novartis Pharma GmbH, Nürnberg, Germany) treatment. This was performed for several reasons: (i) Passive transfer experiments have indicated the existence of a mast cell–activating IgE serum factor in some patients with urticaria factitia (3). As mast cells are activated following mechanical stimulation of the skin, IgE may play a substantial role in the pathogenesis of urticaria factitia. (ii) Omalizumab is licensed for the use in patients with asthma, where it has been demonstrated to be effective and safe. (iii) Finally, omalizumab has also been claimed to protect from symptom development in chronic spontaneous urticaria (4) and inducible urticarias (5, 6).

To our surprise, the patient experienced a major reduction in pruritus and whealing during the first week after initiation of omalizumab (300 mg, s.c.). We continued treatment according to the asthma dosing scheme with 300 mg every 2 weeks. Complete protection

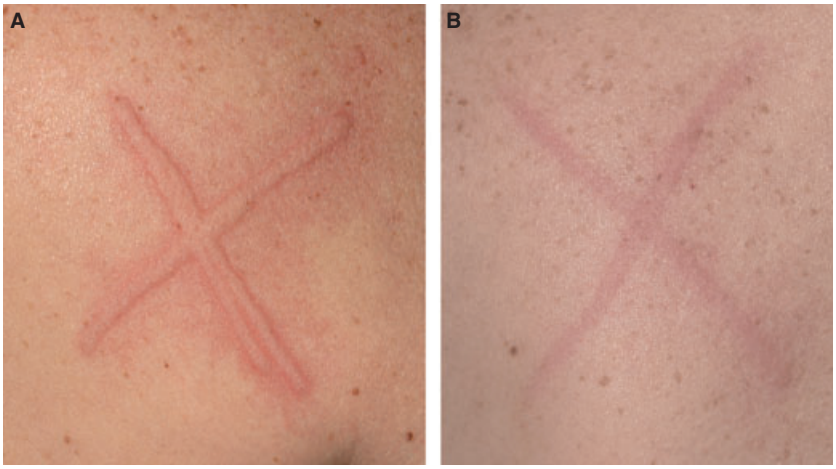


Figure 1 Results of skin testing for dermographism before and after omalizumab therapy. Skin testing using a dermographometer (36 g/mm^2) resulted in wheal and flare reaction associated with severe pruritus before treatment with omalizumab (A). Four weeks after the initiation of omalizumab therapy, the same test did not result in whealing or pruritus, but rather a physiological flare response (dermographism ruber) (B).

from symptom development was achieved in week 4 after the first injection and confirmed by dermographometer testing as shown in Fig. 1.

The reduction in symptoms was accompanied by a remarkable quality of life improvement and cessation of antihistamines and other medication. Although the drug was well tolerated and highly effective, anti-IgE therapy had to be stopped after 3 months because treatment extension for off-label use was denied by the patient's health insurance. Four weeks after the last omalizumab injection, her symptoms recurred and reached a maximum of itching and whealing comparable to the clinical findings before anti-IgE therapy after 6 weeks. We have been trying to obtain permission from the health insurance to reinitiate treatment with omalizumab ever since.

This is – to our knowledge – the first report of successful omalizumab treatment in a patient with urticaria factitia. The rapid and beneficial response to anti-IgE therapy, which was reversed shortly after the end of treatment, supports the role of IgE as a mediator of mast cell activation in urticaria factitia. However, the antigen responsible for IgE-mediated mast cell activation still remains to be identified. Clinical trials with larger patient numbers should be performed to further investigate the value of omalizumab in urticaria factitia and other forms of physical urticaria.

*Department of Dermatology and Allergy
Allergie-Centrum-Charité
Charité – Universitätsmedizin Berlin
Charitéplatz 1,
D-10117 Berlin
Germany
Tel.: +49 30 450 518043
Fax: +49 30 450 518972
E-mail: marcus.maurer@charite.de

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