

7. Nyfeler B, Pichler WJ. The lymphocyte transformation test for the diagnosis of drug allergy: sensitivity and specificity. *Clin Exp Allergy* 1997;**27**:175–181.
8. Baldo BA. Penicillins and cephalosporins as allergens – structural aspects of recognition and cross-reactions. *Clin Exp Allergy* 1999;**29**:744–749.
9. Romano A, Quarantino D, Di Fonso M, Papa G, Venuti A, Gasbarrini G. A diagnostic protocol for evaluating nonimmediate reactions to aminopenicillins. *J Allergy Clin Immunol* 1999;**103**:1186–1190.

Localized cold-induced urticaria associated with specific immunotherapy for tree pollen allergy

J. Ducommun*, V. Morel, C. Ribi, C. Hauser

Key words: cold urticaria; cold-induced urticaria; immunotherapy; localized cold urticaria; physical urticaria.

Cold urticaria (CU, cold-induced urticaria) is a form of physical urticaria characterized by the development of urticaria or

angioedema upon exposure to cold in susceptible individuals (1).

Common

(typical) CU can be divided into either acquired or familial forms. The common acquired forms can be categorized as primary (the majority of cases) or secondary. Secondary acquired CU is most frequently associated with primary and secondary cryoglobulinemia, infectious disease (mainly infectious mononucleosis), drugs, leukocytoclastic vasculitis and neoplasms. Life-threatening anaphylactoid episodes can be induced by sudden total body exposure to cold such as jumps into cold water. Among the atypical CU syndromes, localized CU (LCU) is defined by hives and/or angioedema after cold exposure affecting only a limited skin surface area. Here, we report a

Localized cold urticaria confined to the injection site of tree pollen specific immunotherapy.



Figure 1. Strongly positive ice-cube test on the right arm at the SIT injection site.

patient with LCU associated with subcutaneous immunotherapy (SIT) at the site of the injections.

Perennial specific immunotherapy by subcutaneous injection into the left upper arm with birch and ash pollen extracts (50%/50%, Phostal®; Stallergènes, Antony, France) was started in November 2005 in a 29-year-old man with seasonal rhinoconjunctivitis and asthma. During the second year, SIT with hazel and alder pollen extracts (50%/50%, Phostal®) was added by injecting the right arm because of newly developed allergic respiratory symptoms during the corresponding pollen season. After 1 month of dose increment, the patient experienced itchy weal and flare reactions on the outer aspect of the right upper arm in response to cold exposure (cold shower, air convection). An ice-cube test was strongly positive on the right arm (Fig. 1), weakly positive on the left arm and negative on the forearms, the trunk and the lower extremities. Clinical examination and blood parameter including ESR, red and white blood cell count, immunoelectrophoresis, total

haemolytic complement, C3, C4, cryoglobulin, cryofibrinogen, anti-thyroid antibodies, hepatitis B and C and HIV serology were noncontributory. Antihistamines were prescribed and SIT was continued without subsequent complications or cold-induced symptoms.

Various types of skin injuries can be associated with CU. Common CU has been reported after bee and wasp stings (2) and concurrent to SIT (3). LCU has been observed after ladybird bite (4), dermographic testing, hypothermic skin insults, skin tests with allergens and saline solution, tetanus toxoid injection, surgery and SIT (5, 6). While in some cases with the common form of CU, the phenomenon was transferable with serum and biologic activity associated with IgM or IgE fractions, the underlying mechanisms in LCU are unknown. So far, no primary internal disorders have been reported in this atypical form of CU.

In conclusion, LCU is a rare and benign side-effect of injection SIT which responds to antihistamines, does not

require interruption of SIT and tends to resolve spontaneously.

*Division of Immunology and Allergy
University Hospital
Rue Micheli-du-Crest 24
Geneva 1211
Switzerland
Tel: +41 22 372 9382
Fax: +41 22 372 9369
E-mail: ducommun-julien@diogenes.hcuge.ch

Accepted for publication 7 February 2008
Allergy 2008; 63:789–790
© 2008 The Authors
Journal compilation © 2008 Blackwell
Munksgaard
DOI: 10.1111/j.1398-9995.2008.01697.x

References

1. Kontou-Fili K, Borici-Mazi R, Kapp A, Matjevic LJ, Mitchel FB. Physical urticaria: classification and diagnostic guidelines. An EAACI position paper. *Allergy* 1997; **52**:504–513.
2. Hogendijk S, Hauser C. Wasp sting-associated cold urticaria. *Allergy* 1997; **52**:1145–1146.
3. Anfosso-Capra F, Philip-Joet F, Reynaud-Gaubert M, Arnaud A. Occurrence of cold urticaria during venom desensitization. *Dermatologica* 1990; **180**:276.
4. Roed-Petersen J. Localized cold urticaria. *Contact Dermatitis* 1978; **4**:59.
5. Solomon LM, Strauss H, Leznoff A. Localized 'secondary' cold urticaria. *Arch Dermatol* 1966; **94**:156–160.
6. Garcia F, Blanco J, Perez R, Alonso L, Marcos M, Carratero P et al. Localized cold urticaria associated with immunotherapy. *Allergy* 1988; **53**:110–111.

Omalizumab in persistent severe bakers' asthma

M. Olivieri*, C. A. Biscardo, S. Turri, L. Perbellini

Key words: ACT; bakers' asthma; omalizumab; QoL.

Omalizumab (Xolair) is a humanized monoclonal antibody that binds to free-circulating IgE.

It is indicated for the treatment of severe,

Omalizumab is effective in bakers' asthma.

persistent, inadequately controlled allergic asthma. The efficacy of omalizumab has been confirmed by several studies (1, 2), but it has never been evaluated in severe persistent occupational asthma.

We report on a 53-year-old baker who has been suffering for several years from asthma when exposed to flour dust at the workplace. Respiratory symptoms only partially improved when away from work on holiday and worsened once he returned to work. Skin prick test to bakers' occupational allergens were highly positive to wheat flour and alpha-amylase, occupational aeroallergens to which he is still exposed daily at the workplace. Despite the daily administration of high-dose of inhaled combined fluticasone/salmeterol (2000/200 µg) and montelukast tablet (10 mg), the patient suffered constantly from respiratory symptoms during work. Baseline forced expiratory volume in 1 s (FEV₁) was 59% of predicted normal value and so the patient met the Global Initiative for Asthma definition of severe persistent asthma (3). Taking into account the body weight and total serum IgE level at baseline, the dose of 375 mg of omalizumab was administered by means of subcutaneous injection twice a month. The patient gave his written informed consent and the treatment was approved from the local ethics committee.

Asthma Control Test (ACT), a validated self-administered tool to assess asthma control, was administered at the beginning of treatment and then every month (4). Moreover, asthma-related quality of life (QoL), as determined by the Juniper Asthma Quality of Life Questionnaire (5), based on a Likert scale, was evaluated at the beginning and after 6 months of treatment. The overall ACT score increased gradually from an initial value of 11 up to 25 at the fourth month of treatment and persisted without any change. The QoL result was a remarkable improvement of all individual domains' score (symptoms, activity limitation, emotions, exposure to external stimuli). Montelukast was discontinued after a month and combined fluticasone/salmeterol was gradually reduced every 4 weeks. The therapy with omalizumab was well

tolerated and no asthmatic symptoms were reported even without any changes in the working process. The FEV₁ values (% predicted) progressively increased during treatment reaching reference normal values (up to 98%) after 4 months and remained unchanged despite the interruption of the inhaled therapy. Skin prick test to wheat flour and alpha-amylase were repeated after 6 months of omalizumab treatment revealing the absence of wheal, whereas the histamine-induced wheal persisted without any change.

Our preliminary data suggest the clinical benefit of omalizumab treatment in persistent severe bakers' asthma, a common occupational allergic disease that in many cases necessitates change or loss of job. The cost effectiveness of omalizumab has been demonstrated in patients with severe persistent allergic asthma (6). Actually, this option should be considered in particular when the treatment must be carried out throughout the entire working life. Further trials on occupational IgE-mediated allergic asthma are required to evaluate the cost effectiveness of omalizumab treatment, especially when allergen exposure at the workplace cannot be avoided.

*Department of Medicine and Public Health
Unit of Occupational Medicine
University of Verona
Policlinico "G. Rossi"
Piazza L.A. Scuro, 10
37134 Verona
Italy
Tel: +39 045 8124295
Fax: +39 045 8124974
E-mail: mario.olivieri@univr.it

Accepted for publication 8 February 2008
Allergy 2008; 63:790–791
© 2008 The Authors
Journal compilation © 2008 Blackwell
Munksgaard
DOI: 10.1111/j.1398-9995.2008.01702.x

References

1. Holgate ST, Chuchalin AG, Hébert J, Lötvall J, Persson GB, Chung KF et al. Efficacy and safety of a recombinant anti-immunoglobulin E antibody (omalizumab) in severe allergic asthma. *Clin Exp Allergy* 2004; **34**:632–638.