



Chronic (Cold) Contact Urticaria Treated Successfully with Anti-IgE (Omalizumab)

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Dear Editor,

A 15-year-old male patient presented with complaints of erythema, urticaria and burning on the hands, feet and trunk after contact with cold objects, liquids and/or air for the last two-years. There was no mucosal site involvement and no associated symptoms. The physical examination was normal. The cold provocation test was positive. Biochemistry, hemogram, ESR, CRP, urine analysis, stool examination, latex specific IgE, RF, ANA, skin prick test with common aeroallergens including dust mites, yeasts, animal allergens, various tree and grass pollens, and the serum specific IgE, C3, C4, thyroid function tests, cryoglobulins, cold agglutinins, HIV and HBsAg testing demonstrated normal/negative results. The total IgE level was 5.520 IU/ml in the beginning but decreased to 2.150 IU/ml after 15 months. Due to chronicity of his symptoms and the lack of a triggering factor other than cold, he was diagnosed with type I cold contact urticaria (CCU). Despite using different antihistamines for 10 months, his symptoms have persisted. With the use of subcutaneous omalizumab at the dose of 300 mg/month, the symptoms were under control after 3 months (urticaria activity score (UAS): <6, Table I) and Omalizumab was well tolerated. After 18 months of successful omalizumab treatment, the dose was decreased to 150 mg/month. At the last follow-up, the patient was doing very well and the urticaria was under control.

Chronic cold urticaria (CCU) is one of the inducible (physical) types of chronic urticaria and may appear at any age but peaks in adults, with an incidence of 0.05% in Central Europe and a mild predominance in women (1). CCU comprises roughly 3% of all chronic urticaria patients and is the second most common subtype following symptomatic dermatographism (2). It is defined by the occurrence of a wheal and/or angioedema within minutes following cold contact (objects, liquids, air). CCU symptoms vary from mild, limited wheals to fatal anaphylactic responses due to widespread contact of large skin areas. Acquired CCU is mostly idiopathic or attributed to various infections and cryoglobulinemia. The presence of a cryoprotein might reveal a primary disorder such as essential mixed cryoglobulinemia, hepatitis, autoimmune disease, or lymphoma (3). *PLCG2* gene mutations were newly reported in 3 different families with lifetime CCU (4). This entity must be differentiated from a cold-induced type of cholinergic urticaria, in which urticarial rash develop only when doing exercises in the cold and is not correlated with a positive cold provocation test (3). High IgE levels could be related to primary or secondary immunodeficiency, neoplasia, allergic disorders, skin diseases, infectious/parasitic diseases and inflammatory diseases. There was no clinical and/or laboratory finding suggesting the other diseases mentioned above in the current case. However, some chronic urticaria cases have been associated high IgE levels (5).

Table I. UAS (urticaria activity score) and USS (urticaria severity score) scores before and after the omalizumab therapy

Before Therapy UAS/USS	Anti-IgE Dose 1 UAS/USS	Anti-IgE Dose 2 UAS/USS	Anti-IgE Dose 3 UAS/USS	Anti-IgE Dose 4 UAS/USS	Anti-IgE Dose 5 UAS/USS	Anti-IgE Dose 6 UAS/USS	Anti-IgE Dose 7 UAS/USS	Anti-IgE Dose 8 UAS/USS
28/27	14/16	8/2	8/8	2/4	4/12	2/5	2/2	0/2

CCU and particularly the severe form (type III) has a considerable effect on the patient's quality of life. Since cold exposure, as the trigger of CCU, is hard to avoid in daily life, efficient symptomatic therapy is necessary. Omalizumab (humanized anti-immunoglobulin E) has been demonstrated to be helpful in CCU and could be an attractive choice in the therapy of CCU. So far, some patients with noteworthy and long-term improvement have been reported, while some other studies showed no response to omalizumab treatment (6). Although it has been shown that both 150 and 300 mg doses of omalizumab might work equally in CCU, recent studies suggest using 300 mg monthly for 24 weeks for this disorder (7,8). However, there is no biomarker to predict the response to omalizumab. This case report shows that omalizumab could be useful for the CCU patients.

Keywords: Urticaria, cold urticaria, inducible urticaria, physical urticaria, omalizumab

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