

## Effective treatment of refractory severe heat urticaria with omalizumab

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**Keywords:** anti-IgE; heat urticaria; omalizumab; urticaria.

Heat urticaria is a rare and difficult to treat physical urticaria subtype (1). The first treatment approach is avoidance of heat, which is often not feasible in everyday life.

Based upon casuistic reports, recommended treatment options include

H1-antihistamines, chloroquine, montelukast, and ciclosporin A (2).

We present complete symptom relief of a severe treatment – refractory heat urticaria with omalizumab 450 mg biweekly.

A 42-year-old male presented with a 3-year history of severe, often generalized heat urticaria occurring several times a day, in part associated with angioedema and dyspnea. Several times he received hospital emergency treatment, suffered from significant reduction of quality of life and was

not able to work as a mechanist. From his 17th year of life, a hypogonadism is being treated with testosterone every third month but without any association to the heat urticaria.

The standardized warm arm bath caused hives at the category temperature of 38°C. In addition, provocation with warm air resulted in localized urticaria.

An extensive diagnostic work-up did not show any trigger factor besides elevated total IgE (429 kU/l, Immulite 2000, DPC, Biermann GmbH, Bad Nauheim, Germany), without detectable specific IgE antibodies (Sx1, UniCAP250, Phadia). The autologous serum skin test with serum at room temperature and heated to 40°C was negative. Lab results, skin prick tests with common allergens, upper and lower GI-endoscopies, rheumatologic and neurologic diagnostic procedures

were normal. Therapeutic regimens with different H1-antihistamines each in up to fourfold dosage, addition of montelukast (10 mg), ciclosporin A (2.5 mg/kg for 6 weeks), or chloroquine (250–500 mg/d for several months) did not cause improvement. High (50–250 mg prednisolone per day) but not lower doses of corticosteroids resulted in slight improvement.

Because of the severity and refractory and the successful reports of omalizumab in cold urticaria (3), solar urticaria (4), cholinergic urticaria (5), and chronic spontaneous urticaria (6), we initiated off-label treatment with omalizumab after informed consent.

At the beginning, the patient received alternating subcutaneous injections of 300-mg and 450-mg omalizumab biweekly (calculated dose according to asthma table: 375 mg). After the first dose, the

**We report for the first time successful treatment of refractory severe heat urticaria with omalizumab.**

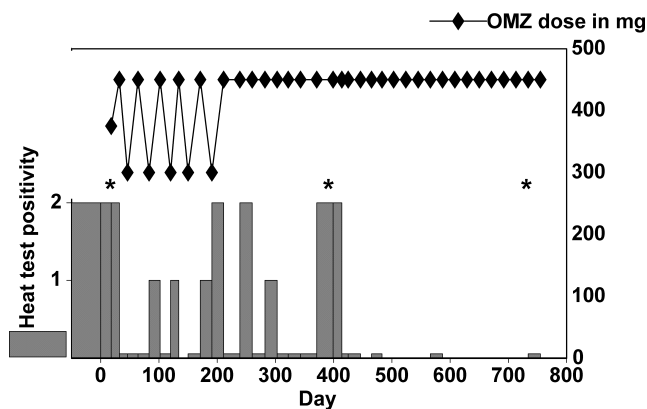


**Figure 1** Course of heat test positivity (gray bars) using warm arm bath (left y-axis: 0, negative; 1, single hives at 42 °C; 2, several confluent hives at 38 °C) in response to omalizumab (OMZ) dose in mg (♦) shown on the right y-axis. Stars (\*) indicate hot summer months.

patient reported slight symptom improvement of his heat urticaria. The second dose of omalizumab resulted in considerable improvement (Fig. 1). Only after four applications, the patient was almost free of symptoms and could reconvene working. He reported better improvement after the 450-mg dose compared to the 300-mg dose, and this observation was confirmed by challenge test results (Fig. 1). Therefore, from the 12th injection on, we applied the 450-mg omalizumab dose biweekly. However, the attempt to extend the application interval to 3 weeks after 18 injections (Fig. 1) resulted in worsening of symptoms. Currently, the patient received more than 38 applications without any side-effects and remains almost free of symptoms at a dose of 450-mg omalizumab biweekly without any comedication.

To the best of our knowledge, this is the first description of a significant beneficial effect of omalizumab in severe heat urticaria. The detailed pathogenesis of heat urticaria is not known. Although at the moment chronic spontaneous and physical urticaria types are not regarded as IgE-mediated diseases,

anti-IgE treatment appears to be effective. In chronic spontaneous urticaria, only one total nonresponder to omalizumab has been described so far (6). However, the exact therapeutic mechanism is unclear. Our case indicates a rather symptomatic than causal effect. Future controlled studies will have to clarify the active principle as well as the optimal dose and duration of treatment with omalizumab in different urticaria subtypes.

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