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Giovanna Malara & Claudio Sciarrone

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ARTICLE



Chronic spontaneous urticaria treated with omalizumab: report of two cases

Giovanna Malara and Claudio Sciarrone

Department of Dermatology, Papardo Hospital, Messina, Italy

ABSTRACT

Background: Chronic spontaneous urticaria (CSU) is a relatively common skin disease whose etiopathogenesis, as well as other factors influencing disease manifestations, are not fully understood. Mast cell function is recognised as having a central role in CSU signs and symptoms.

Therapeutic options are limited; a number of drugs, recommended by international guidelines for the management of urticaria, lack regulatory approval for CSU and are prescribed off label.

Omalizumab, a recombinant humanized anti IgE antibody, has recently received the approval for CSU treatment in Europe after an appropriate clinical development.

Patients and results: Two case reports, that describes our encouraging experience with this therapeutic option in a real-life setting are discussed and deeply investigate the different scenario for the omalizumab use.

Conclusion: In both cases, a complete remission of CSU symptoms after omalizumab treatment are demonstrated. Moreover, 6 months therapy gave the better results, with a relapse, in one subject, 1 month after discontinuing omalizumab. Accordingly, a better understanding of long-term safety and efficacy should be needed to allow long-term administration in responding patients through a changing in prescription rules.

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Omalizumab; chronic spontaneous urticaria; IgE blocker

Introduction

Chronic spontaneous urticaria (CSU), formerly known as chronic idiopathic urticaria and chronic urticaria (CU), is one of the most frequent skin conditions affecting up to 20% of the population in the world (1). It is more frequent in females than in males (female/male ratio 2:1), and although it can affect all ages, most cases occur in people between 20 and 40 years old (1). This condition is characterized by recurrent eruptions of superficial wheals (commonly referred to as hives) together with erythema and itching, occurring over a period of at least 6 weeks. Single wheals typically disappear within 12 h from occurrence (2,3), and the disease may recur for decades (4–6). The whole skin surface and mucous membranes may be involved.

CSU has a considerable impact on health-related quality of life (7). In addition, CSU is associated with direct and indirect health-care cost increase, as well as reduced work and daily life performance (3).

Several factors seem to have a role in urticaria physiopathology, such as autoimmune disorders, mast cells abnormalities, and chronic infections (1,8–10). Indeed, recent evidences support the possible role of IgE (also in monomeric form) in modulating mast cells granules release threshold, possibly through their link with either FcεRI or other receptors (11). It is possible to interfere with this mechanism by targeting IgE and thus limiting their interaction with mast cells.

Management of CSU is challenging and often disappointing. Current guidelines of the European Academy of Allergy and Clinical Immunology (EAACI)/Global Allergy and Asthma European Network (GA²LEN)/European Dermatology Forum (EDF)/World Allergy Organization (WAO) recommend a stepwise approach based on second-generation non-sedating oral H1-antihistamines as first-line treatment for urticaria. In most patients, symptoms

persist despite the standard dosing of antihistamines. Upon failure, doses of H1-antihistamines should be increased up to four-fold. Resistant patients should receive a third step treatment with non-antihistamine drugs that include cyclosporine, leukotriene receptor antagonists (LTRA), or omalizumab. Omalizumab is a humanized anti-IgE antibody that has been recently approved for the treatment of resistant CSU (12).

The effectiveness of omalizumab in the treatment of two patients with CSU, resistant to standard therapy, is described.

Case reports

Case report 1

A 32-year-old female was admitted, for the first time, to our outpatient center, as previously reported (13). She had suffered from a severe urticaria with recurrent and frequent episodes of diffused erythema and short-lived wheals (Figure 1(a)) and severe itching, for several months.

Urticaria Activity Score in the last 7 days (UAS7) = 28 was recorded. The patient seemed in good health and had no previous history of seasonal allergies or other allergic complaints.

The hematological values were normal, except a slight increase of neutrophils, complement C4, total IgE, and reactive C protein (RCP) levels. Skin prick tests for common allergens were negative.

The patient had received methylprednisolone 16 mg/day and levocetirizine 5 mg/day for a long time, with any improvement in urticaria severity and episodes frequency. The chronic intake of systemic steroids had caused a remarkable increase in body weight and gastritis had been present in the last 2 months, as expected (14).

Cyclosporine (CsA) 3 mg/kg/day and levocetirizine 5 mg/day were prescribed. Efficacy was judged very low after a few weeks.

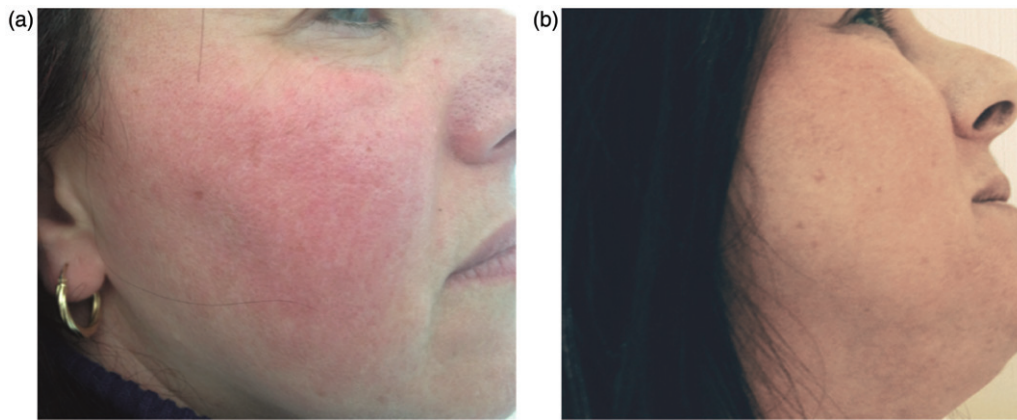


Figure 1. Case report 1. (a) wheals observed at first visit; (b) symptoms improvement after omalizumab treatment.

The patient reported a short period of improvement at the beginning of the new therapy, followed by new, frequent, urticaria episodes. Significant sleepiness was reported from the patient; therefore, increasing the dosage was not achievable.

Because of the low effectiveness of previous treatments, omalizumab 300 mg was administered subcutaneously. CSU completely disappeared 2 days after omalizumab administration. The treatment continued for 6 months as recommended, with a value changing from basal UAS7 = 5 to UAS7 = 0, at the end of treatment. A good remission of facial symptoms is shown in [Figure 1\(b\)](#). Therapy was stopped and it had not been reinitiated at the time this report was written, 1 year later, with a complete remission of the disease: no relapse was observed, the patient no longer showed wheals.

Case report 2

A 45-year-old man with 2 years of chronic urticaria, without any concomitant diseases, visited our center, and a UAS7 = 31 was recorded (13). Prick tests for common allergens, enzyme immunoassays, and autologous skin tests were negative. Standard laboratory examinations, including thyroid hormones, a chest X-ray, dental orthopantomography, and urea breath, were normal.

Total serum IgE level was 500 kU/L; the levels of IgE and anti-FcεRI antibodies could be considered biomarkers for the effectiveness of omalizumab, as previously suggested, even if the concomitant use of corticosteroid may represent a bias (15).

The patient had previously received several treatments, including systemic corticosteroids (methylprednisolone 16 mg/day for 10 days; then 8 mg/day for 7 days and finally 4 mg/day for two weeks), antihistamines (initially at the standard dose and then four-doubled), antileukotrienes (10 mg/day without any improvement in symptoms) and CsA (3 mg/kg/day), that had provided only temporary and partial symptoms resolution.

The patient underwent omalizumab therapy (300 mg subcutaneously every 4 weeks) and a few days after the first administration he achieved a rapid improvement in signs and symptoms of urticaria. He was treated with omalizumab for 6 months. The patient had relapsed 1 month after interrupting urticaria treatment. Urticaria disappeared again as soon as omalizumab therapy was resumed.

The patient completed the whole cycle of the treatment and, up to now, he does not refer new wheals and have a good control of the disease. No side effects, for omalizumab treatment, were reported, in both the case reports.

Discussion

Current EAACI/GA²LEN/EDF/WAO guidelines recommend second-generation non-sedating oral H1-antihistamines as a first line treatment for urticaria. Nevertheless, in most patients symptoms persist despite standard dosing of antihistamines (12).

Omalizumab is a 149-kDa humanized monoclonal antibody obtained using recombinant DNA technology. It is an IgG1 type antibody composed of human (95%) and murine (5%) fractions (5). The latter is the active fraction, which also prevents anaphylactic responses (16).

Omalizumab has recently been approved for the treatment of CSU (7,17). It acts on several factors that play a major role in the physiopathology of urticaria: it blocks the binding of IgE to FcεRI, reducing mast cell sensitization, free plasma IgE, and the number of FcεRI receptors on the surface of mast cells and basophils (18). In addition, some laboratory data suggested that the omalizumab mechanism of action is multifactorial and that the drug might even targeted cells such as CD4⁺ T lymphocytes and B cells (19).

Several clinical trials demonstrated a good safety profile for omalizumab (7). Nevertheless, omalizumab does not change the natural history of CSU; responding patients suffer relapse after treatment interruption in a variable period. Recently, results from the XTEND-CIU (Xolair Treatment Efficacy of LoNger Duration in Chronic Idiopathic Urticaria) Study showed that continued treatment with omalizumab prevented relapse and improved quality of life and that re-treatment, if needed, was safe and effective (20).

In conclusion, clinical practice is confirming the efficacy and tolerability of omalizumab for the treatment of resistant CSU that is a frequent and challenging disease for the dermatologist. A better schedule of administration should be available for relapsing patients.

Patient consent

The patients gave consent to the inclusion of material pertaining to themselves into this article, they acknowledged that they cannot be identified via the paper; the Authors fully anonymized patients material.

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Disclosure statement

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