

# Omalizumab for urticaria treatment in clinical practice: a case series

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## Abstract

**Introduction:** Omalizumab (Xolair) originally intended to reduce symptoms of moderate to severe asthma uncontrollable with steroids is the first monoclonal antibody approved for treatment of chronic spontaneous urticaria in 2014.

**Aim:** To evaluate response and potential side effects to omalizumab treatment in clinical practice.

**Material and methods:** Eleven patients (6 males and 5 females) were recruited into the study. All participants signed written informed consent before enrollment to the study. At the beginning they were receiving 300 mg of omalizumab in a subcutaneous injection every 4 weeks in an outpatient clinic. Five the clinical response was sufficient, the dose of omalizumab was decreased to 150 mg. We evaluated response to the treatment using the Urticaria Activity Score in the last 7 days and the Urticaria Control Test at certain time points.

**Results:** Nine out of 11 patients achieved complete syndrome resolution. Five patients achieved clinical remission after the first dose of omalizumab. Mean time to remission was 9.3 weeks. During the study, no side effects were observed.

**Conclusions:** Omalizumab appears to be a safe drug, which in a quick and effective way induces remission in patients who have not responded to previous treatment.

**Key words:** urticaria, omalizumab, chronic spontaneous urticaria.

## Introduction

Chronic spontaneous urticaria affects about 1% of the population and is defined as the presence of the clinical signs of urticaria lasting for at least 6 weeks. Omalizumab (Xolair<sup>®</sup>) was originally intended to reduce symptoms of moderate to severe asthma uncontrollable by steroids. It became the first monoclonal antibody approved for the treatment of chronic spontaneous urticaria (CSU) by the US Food and Drug Administration and the European Medicines Agency in 2014. According to the European Academy of Allergy and Clinical Immunology's guidelines on CSU, omalizumab should be used as the third line treatment after an insufficient response to the second-generation H1-blockers (antihistaminics – AH), leukotriene-receptor-antagonists (LTRA), cyclosporine A (CSA) or corticosteroids (also known as cortisone-like medicines – CLM) [1]. Omalizumab inhibits the binding of IgE to FcεRI on basophils and mast cells by binding itself

to Fc portion of IgE at the same place where IgE binds to FcεRI. The repetitive administration of omalizumab leads to IgE depletion and down-regulation of FcεRI on basophils and mast cells, which make them less sensitive to allergen stimulation. The efficacy of omalizumab has been proven in several clinical studies using 150–600 mg doses, although data concerning omalizumab usage in clinical practice are still limited [2–7]. We present the case of 11 patients with CSU who had unsatisfactory response to the other types of the recommended treatment and began the treatment with omalizumab.

## Aim

A retrospective evaluation of the response to treatment and potential side effects during omalizumab treatment in clinical practice.

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## Material and methods

A group of 11 patients (6 males and 5 females) at the (mean  $\pm$ SD) age of  $46.54 \pm 10.68$  were recruited into the study. All participants signed written informed consent before enrollment to the study. Median length of CSU was 23.5 months. At the beginning, they were receiving 300 mg of omalizumab (Xolair®; Novartis, Basel, Switzerland) in a subcutaneous injection every 4 weeks in an outpatient clinic. If the clinical response was sufficient, the dose of omalizumab was decreased to 150 mg. We evaluated the response to the treatment using the Urticaria Activity Score in last 7 days (UAS7). The Urticaria Control Test was performed (UCT) [6] before the drug administration, after 12 weeks from the beginning of the treatment and at the end of treatment. The UAS7 rating of the severity of clinical signs ranged from 0 to 3 (0 – none; 1 – mild; 2 – moderate; 3 – intense, total score ranging from 0 to 6) and the score was a sum of the everyday scores from the previous week (maximum score – 42), which was calculated by the use of patients' diaries. Whereas, the UCT evaluated the control of urticaria on a 4-point scale (0 – very much; 1 – much; 2 – somewhat; 3 – a little; 4 – not at all); total score ranging from 0 to 16). The complete urticaria resolution was defined as UAS7 = 0.

## Results

Nine out of 11 patients achieved complete syndrome resolution. Five patients achieved clinical remission after the first dose of omalizumab. The mean time to remission was 9.3 weeks. During the study, no side effects were observed. Complete group characteristics are presented in Table 1. The changes in UAS7 and UCT scores are shown in Figures 1 and 2.

## Discussion

The presented case series includes 11 patients suffering from therapy-resistant chronic urticaria. Each patient received one dose of 300 mg, which was then reduced to 150 mg if the patient's response was satisfactory. We have proved that lowering the initial dose of omalizumab was sufficient to reduce the severity of urticaria in 9 out of 11 patients. We did not observe any side effects. Our results are consistent with other existing data about using omalizumab in CSU treatment.

Saini *et al.* [2] performed a multicenter, randomized, double-blinded study on 90 patients with chronic urticaria not responsive to the classical treatment. They showed the clinical efficacy after only one dose of omalizumab. A relief of symptoms compared to placebo was statis-

**Table 1.** Clinical characteristics of the study group

No.	Sex/age	Disease duration	Type of chronic urticaria	Previous treatment	Treatment duration (approximated to months)	Number of 150 mg doses	Number of 300 mg doses	Time to remission [weeks]
1	F/59	8 months	Pressure urticaria	AH, CLM	14	14	0	4
2	F/32	3 months	Spontaneous urticaria	AH, CLM, LTRA	15	14	1	4
3	F/49	8 years	Cold urticaria	AH, LTRA, CSA, chloroquine	8	7	1	4
4	F/56	2 years	Spontaneous urticaria	AH, CLM, LTRA, CSA	6	5	1	4
5	F/33	31 years	Spontaneous urticaria	AH, CLM, LTRA	12	11	1	52
6	M/60	6 years	Spontaneous urticaria	AH, CLM, CSA, azathioprine	22	8	14	16
7	M/45	1 year 4 months	Cold urticaria	AH	7	2	5	No remission
8	M/60	15 years	Spontaneous urticaria	AH, CLM, LTRA	9	8	1	4
9	M/45	6 months	Spontaneous urticaria	AH, CLM, LTRA, CSA	9	8	1	8
10	M/41	7 years 5 months	Cold urticaria	AH, LTRA, sulfasalazine, CSA	8	5	3	24
11	M/32	1 year 11 months	Spontaneous urticaria	AH, CLM, LTRA, CSA, azathioprine	6	5	1	32

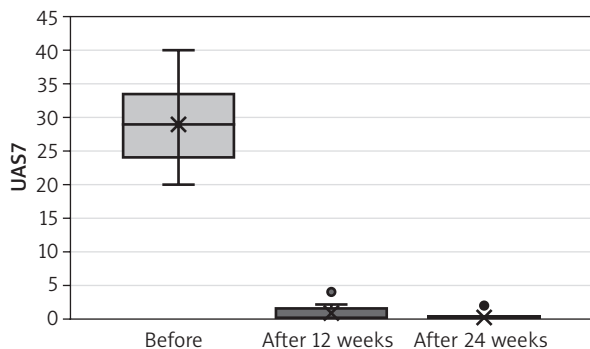


Figure 1. The UAS change during the treatment

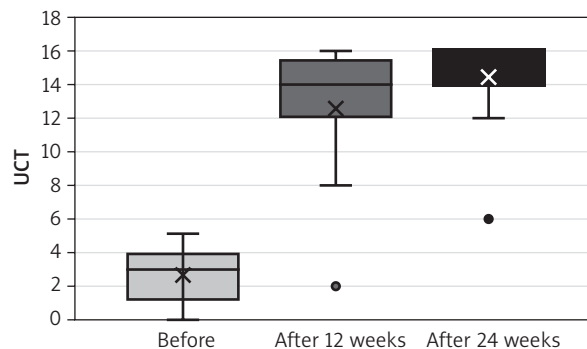


Figure 2. The UCT change during the treatment

tically significant for the dose of 300 mg and 600 mg. There was no significant improvement after using a dose of 75 mg. After 2 weeks, a complete resolution of symptoms was achieved in 36% of patients in the 300 mg group, 28.6% in the 600 mg and 4.4% in the 75 mg and 0% in the placebo group. Their results were confirmed by Maurer *et al.* [3] in the randomized multicenter study on 323 patients who received injections of omalizumab every 4 weeks. They observed that the dose of 300 mg improved the course of urticaria in 44% of patients, 150 mg in 22%, 75 mg in 16% and placebo in 5% [3].

Currently, the data on the long-term safety of omalizumab in the CSU treatment are scarce. Our study has shown that treatment with omalizumab was well tolerated and efficient in almost all patients who failed with therapy with antihistamines, corticosteroids, CSA or azathioprine. The most common side effects after omalizumab administration include allergic reactions at the injection site, a headache, a fever and abdominal pain. However, most of these reactions are mild and acceptable for the patients. The risk of serious side effects has been established between  $\geq 1/1,000$  to  $< 1/100$ . However, based on the bronchial asthma cohort studies, it can be expected that omalizumab is secure in both adults and children [8].

## Conclusions

Many previous studies have shown the efficacy of omalizumab in the treatment of spontaneous urticaria. In summary, omalizumab appears to be a safe drug, which in a quick and effective way induces remission in patients who have not responded to the previous treatment. Although omalizumab is a drug also used for other indications, the exact mechanism of action remains unknown. It should be also determined how long omalizumab should be used after achieving remission to sustain the clinical response. Another interesting issue is to identify the exact cause of treatment failure in some patients. Despite many questions and uncertainties, omalizumab should be considered in every classical treatment failures.

## Acknowledgments

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## Conflict of interest

The authors declare no conflict of interest.

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