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Letter to the editor

Effective treatment of different phenotypes of chronic urticaria with omalizumab: Case reports and review of literature

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Abstract

Despite the excellent efficacy and safety profile of omalizumab in chronic spontaneous urticaria (CSU), there are scarce data concerning its role in the treatment of refractory cases with different phenotypes of urticaria. We describe our experience with the therapy of nine patients with CSU co-existing with delayed pressure urticaria (DPU) or angioedema or both and refractory to treatment with high-dose antihistamines. The first patient, with severe CSU and recurrent angioedema, did not respond well to cyclosporine A or corticosteroids and suffered from numerous side effects of long-term corticosteroid therapy. The second patient presented with severe symptoms of DPU, which first of all prevented any daily activities of the professional routines. Both patients showed a complete remission of urticaria after the first injection of omalizumab. The third patient with CSU and severe DPU had been ineffectively treated for more than 20 years with various medications. Following the administration of omalizumab, the symptoms of CSU subsided but those of DPU intensified, and the drug was withdrawn after two cycles. In another four patients with refractory CSU and angioedema, the symptoms subsided after the first administration of omalizumab, and the patients have been in remission for about 5 weeks. In the remaining two patients, the symptoms did not resolve despite four 300 mg doses of omalizumab. It is important to establish a therapeutic regimen with omalizumab (150–300 mg; every 4–8 weeks) tailored to individual patient's needs and dependent on the type of urticaria; this may minimize unnecessary the medication exposure, adverse drug effects, and healthcare costs.

Keywords

chronic spontaneous urticaria, delayed pressure urticaria, omalizumab

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Introduction

Chronic urticaria is a heterogeneous disorder, which may be either spontaneous or induced. The disorder is most probably caused by an interactive combination of immune, genetic, and environmental factors, including infections and is associated with the activation of immune/inflammatory, coagulation/fibrinolytic, and neurohormonal processes.[1–9]

The current guidelines recommend second-generation non-sedating H_1-antihistamines (nsAHs) as the mainstay of treatment. However, more than half of the patients continue to develop symptoms despite the use of standard doses, and in such cases, an up to four-fold increase in the dosage (off-label therapy) is recommended as the second-line option. In patients with chronic urticaria who do not respond to antihistamine treatment, omalizumab,

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cyclosporine A, or montelukast is recommended as the third-line therapy. In addition, corticosteroid (CS) treatment may be considered during the exacerbation of symptoms. However, anti-inflammatory and immunomodulatory therapies may be unsuitable for long-term use owing to considerable side effects and concerns about the risk:benefit ratio.[10,11] Among anti-urticarial medications, only antihistamine drugs in licensed doses and omalizumab have been approved for use in chronic spontaneous urticaria (CSU) by local agencies for the registration of medicinal products. Therefore, there has been an increasing interest in the use of omalizumab as a well-tolerated and effective option for inducing and maintaining long-term remission in patients with refractory CSU, regardless of the dosing protocol or the immune status, age, or sex of the patients.[11–14]

Despite the excellent efficacy and safety profile of omalizumab in CSU, there are still scarce data concerning its role in the treatment of refractory cases with different phenotypes of urticaria. Therefore, the aim of this paper was to describe our experience in the treatment of patients with CSU and delayed pressure urticaria (DPU) refractory to treatment and to discuss the use of omalizumab in this context.

Patients

We report a retrospective case series of nine patients with persistent symptoms of difficult-to-treat CSU co-existent with DPU or angioedema or both and treated with omalizumab.

Attempts to control the disease with antihistamines and, in some cases, with low-to-moderate doses of CSs, cyclosporine, or other immunosuppressive and immunomodulatory drugs were either unsuccessful or led to unacceptable side effects. A complete response was defined as no symptoms and no need for the use of medications.

At the beginning of the treatment, the quality of life index of our patients was in the range of 11–27 (very large to extremely large effect), using the Dermatology Life Quality Index (DLQI), and the urticaria activity score for the preceding 7 days (UAS7) was in the range of 35–42 (severe activity). In all patients, skin biopsies of urticarial lesions were taken, and histological analyses were performed to exclude urticarial vasculitis. Each patient underwent the following investigations: (1) routine laboratory tests (full blood count, erythrocyte sedimentation rate, C-reactive protein, glucose, hepatic function; serum and plasma levels of creatinine, immunoglobulins, and complement; urine analysis); (2) measurement of antibodies: antinuclear (EUROLINE ANA Profile 3; Euroimmun), antitransglutaminase, antithyroid, against *Borrelia burgdorferi*, *Ascaris lumbricoides* and *Toxocara canis*, specific immunoglobulin E (IgE) against food and inhalant allergens in serum or plasma; (3) other tests (testing for antistreptolysin O, syphilis, rheumatoid factor, hepatitis serology as well as stool examinations for ova, parasites, and *Helicobacter pylori* antigen). In addition, patients were referred for dental and ear, nose, and throat consultations and underwent abdominal ultrasonography.

The autologous serum skin test for autoreactivity was performed in six patients. The results were positive in four patients and negative in two patients. Two patients suffered from Hashimoto disease. Other relevant co-morbidities were excluded.

Patient 1

A 34-year-old woman presented to our urticaria unit with a 3-year history of severe, difficult-to-treat CSU with angioedema and DPU. The major clinical issues in the patient were poorly controlled CSU and frequently recurring symptoms of angioedema. No evidence of an underlying disease was found.

The patient had undergone treatment with antihistamines at a four-fold higher dose compared with the standard dose, alone and in combination with montelukast, cyclosporine, and CS, but the therapy failed to control the disease activity. She suffered from a broad spectrum of side effects of long-term CS therapy (including weight gain, depression, headache, dyspeptic symptoms, mood changes, and Cushingoid appearance).

By the time of her referral to our clinic, the patient had been treated with dexamethasone (up to 2 mg/d) and a high dose of nsAHs. During the exacerbation of symptoms, she received higher doses of CSs, which allowed to reduce the frequency of angioedema from the average of twice a week (mainly lips and throat) to the average of once a month. In addition, skin symptoms were alleviated (mainly itch), and their reduced

severity could be tolerated by the patient (UAS7, 28–34). Higher CS doses were not well-tolerated by the patient and did not significantly reduce the symptoms.

Before starting anti-IgE therapy, the patient's total IgE levels were 145.7 kU/L. To our surprise, after the first administration of omalizumab (300 mg subcutaneously), urticaria symptoms resolved within 2 days. In addition, the patient could discontinue all concomitant medications (nsAHs and CSs).

Importantly, during the 3 years of disease duration, the patient had not experienced a remission of symptoms. Omalizumab was administered again at a dose of 300 mg after 4 weeks. The treatment regimen was continued with a dose reduction to 150 mg and longer periods in-between subsequent injections: third injection after 4 weeks (150 mg) and fourth injection after 6 weeks (150 mg). After all four injections, anti-IgE therapy was stopped owing to a complete remission of urticaria and angioedema symptoms.

The symptoms recurred after 7 weeks although they were insignificant and did not require the use of nsAHs (UAS7, 6). The fifth injection of omalizumab (150 mg) was administered, and the symptoms resolved completely within 2 days as observed after the first injection. They again recurred after 6 weeks; the sixth dose of omalizumab (150 mg) was injected, and the symptoms resolved again within 2 days. When they recurred after 5 weeks, the seventh injection (150 mg) was administered. A decision was made to administer omalizumab again if the symptoms recurred. The regimen was continued with the cycles of omalizumab (150 mg) administered every 5–6 weeks.

Patient 2

A 23-year-old woman presented with a 1-year history of severe DPU and CSU with angioedema and severely impaired quality of life. Before the referral to our urticaria clinic, she had been treated with antihistamines at a dose of up to four-fold higher than the recommended dose in combination with CS, but without significant effects. The major issue in this patient were the symptoms of DPU that limited her daily activities including those in her professional life (use of dental equipment). Prednisone at a dose of up to 20 mg significantly reduced skin lesions and angioedema, but it only partly reduced edema of the hands and feet and did not prevent the recurrence of symptoms. Higher prednisone doses resulted in a complete resolution of symptoms but were badly tolerated by the patient because of more severe dyspeptic symptoms despite the use of proton-pump inhibitors.

Before starting anti-IgE therapy, the patient's total IgE level was 43.86 kU/L.

Similarly to the first case report, already 2 days after the first injection of omalizumab, all symptoms of DPU and CSU completely resolved, and the patient was able to resume all activities. She discontinued all other medications and did not develop any symptoms of CSU and DPU. After 4 weeks, the second injection of omalizumab (150 mg) was administered.

After two injections, anti-IgE therapy was stopped because of complete symptom remission, and a decision was made to restart the therapy if the symptoms recurred. The patient developed symptoms of urticaria again after 8 weeks since the administration of the second dose of omalizumab. We administered the drug again at a dose of 150 mg and achieved a complete remission within 2 days. After 7 weeks, urticaria manifested itself again, and the fifth cycle of omalizumab (150 mg) was administered again with the complete remission of symptoms within a few days. The regimen was continued with the cycles of omalizumab (150 mg) administered every 7–8 weeks.

Patient 3

A 59-year-old male patient with the symptoms of severe DPU co-existent with CSU had been ineffectively treated for more than 20 years with antihistamine, anti-inflammatory, immunomodulatory, and immunosuppressive drugs (sulfasalazine, histaglobulin, cyclosporine A, dapsone, cyclophosphamide, methotrexate, azathioprine, leukotriene receptor antagonists, non-steroidal anti-inflammatory drugs, and CSs). Despite receiving such a regimen, the everyday functioning of the patient was severely impaired. Severe symptoms of DPU significantly limited his daily activities owing to painful swellings occurring even after light pressure. During surgery, edema and loosening of stitches were observed at the site of an incision. The patient received an additional treatment because of non-viral chronic hepatitis (probably drug-induced), hypertension, and type 2 diabetes.

At present, his symptoms are only partly controlled by means of a long-term use (more than 10 years) of methylprednisolone at a dose of 16 mg and fexofenadine at a dose of 180 mg twice daily. Because none of the previous treatment strategies had resulted in an improvement of CSU symptoms, we started omalizumab treatment. After two cycles of omalizumab at a dose of 300 mg at an interval of 4 weeks, a remission of CSU symptoms was observed while the symptoms of DPU persisted and, according to the patient, became even more severe. The treatment with omalizumab was discontinued.

Patients 4 and 5

A 44-year-old male patient and a 31-year-old female patient were admitted with severe CSU and frequently recurring symptoms of angioedema, which could not be controlled with higher than standard doses of antihistamine drugs and leukotriene receptor antagonists. To obtain at least a partial control of symptoms, both patients regularly received prednisone at a dose of 10 mg, which was increased to 20–40 mg during the periods of more exacerbations. The patients received four injections of omalizumab (300 mg every 4 weeks) but their symptoms remained uncontrolled. Therefore, cyclosporine was introduced but the therapy was discontinued after 1 month because of adverse effects.

Patients 6, 7, 8, and 9

Four patients aged of 39, 24, 55, and 64 years, with CSU and angioedema and without remission on high doses of antihistamine drugs, were admitted to our clinic. They have received a CS (prednisone, up to 15 mg) for the past 3–10 years. We observed a complete remission of symptoms after 1 dose of omalizumab (300 mg) within 24–48 h. The regimen was continued with the individual cycles of omalizumab (150–300 mg) administered every 5–6 weeks.

Discussion

The cases described above show that both CSU and DPU with co-existent angioedema can be quickly and successfully treated with omalizumab without side effects. Of nine patients, six achieved a complete control of urticaria and angioedema after the first injection of omalizumab. Importantly, six of our patients reported a quick and complete relief of symptoms within a few days (up to 3 days) after the initial injection. Similar observations were reported previously.[12–14] All of those patients received numerous treatments in the past, which were either unsuccessful or caused unacceptable side effects.

Efficacy of omalizumab in chronic urticaria

It is now clear that omalizumab therapy allows to achieve remission, which is particularly important in patients with severe disease activity owing to distressing symptoms, significantly reduced quality of life, and adverse effects of previous treatments, typically a long-term use of CSs or cyclosporine or both.[11–14]

Omalizumab has been shown to be highly effective and to induce clinical remission in 40–83% of the patients, often within a few days.[12–15] In a large randomized, double-blind, placebo-controlled trial, Kaplan et al.[15] demonstrated that approximately half of the patients who received add-on omalizumab achieved a UAS7 of 6 or lower, and one-third of the patients were completely free from itch and hive (UAS7 = 0, denotes a complete resolution of symptoms, which represents the most desirable outcome). On the other hand, in a retrospective clinical analysis of data from 1250 injections administered over 4 years to 51 patients treated outside of clinical trials, omalizumab treatment led to a complete remission in 83% of patients with CSU and 70% of those with induced urticaria, including 88% of cases with DPU.[13] However, there is still a number of patients who do not benefit from omalizumab treatment. In our case series, two patients who received omalizumab (300 mg) every 4 weeks (a total of four doses) did not achieve remission (measured by UAS and DLQI) and had to continue the first-line treatment.

Omalizumab therapy: Dosing and regimen

Large controlled trials on the treatment of CSU showed the efficacy both of 150 mg and 300 mg of omalizumab administered every 4 weeks.[12,14,15] It is still unclear how to reduce the dose and extend dosing intervals in patients who achieved a complete remission. Apart from the data on the beneficial dosage, there is no standard protocol for the

dosing intervals and duration of treatment. The available literature describes algorithms both with the stable doses of omalizumab administered at regular intervals as well as those in which dosing intervals are gradually extended and omalizumab dose is reduced so that the patient remains asymptomatic during treatment.[13,16,17] The need for an individualized approach is emphasized because patients differ in terms of the clinical course of the disease and response to treatment.[16] The individualized approach to the treatment of urticaria with omalizumab has been proved effective, well-tolerated, more cost-efficient, and more convenient for the patient.[13,16] In our practice, we use this regimen with some modifications. Once a complete response has been achieved, we continue to administer omalizumab on an irregular basis and wait for hives to reappear. We administer the lowest possible doses (a minimum of 150 mg) at the longest possible intervals depending on the recurrence of symptoms.

We observed that the symptoms of chronic urticaria may recur at different time intervals after consecutive injections. On relapse, the severity of symptoms is low and does not require the use of antihistamine drugs in the initial phase. Importantly, such a regimen does not worsen the patient's quality of life. In addition, the patient is convinced about the necessity to take subsequent doses owing to the recurrence of symptoms. The cost-effectiveness of such a regimen is also important because it allows to use the therapy in a larger number of patients.

There are currently no data in the literature suggesting that continuing the treatment with a stable dose of omalizumab every 4 weeks for a longer period of time (in a patient with a complete remission) has beneficial effects on the natural course of the disease and long-term remission after the discontinuation of treatment. Therefore, from the economic and clinical perspectives, it seems rational to try and extend dosing intervals in all patients with partial or complete remission.[16]

Suggested treatment algorithms based on our own experience and the available literature

Usually, the starting dose of omalizumab is 150 mg, and if the symptoms resolve completely, the subsequent dose is administered on symptom recurrence. In patients with severe symptoms and a poor response to CS treatment, the starting dose of omalizumab is 300 mg. If remission is achieved, a reduced dose of 150 mg is administered after 4 weeks. If remission continues, the next dose is administered only after the symptoms of urticaria have recurred. The recurrence of symptoms after a dose reduction indicates that the dose has to be increased again to 300 mg. If the remission cannot be achieved on the 150-mg dose, the dose should be increased to 300 mg after 4 weeks. If symptoms persist, the 300-mg dose should be administered every 4 weeks for 8–12 weeks. If no remission is observed after that period, the therapy should be discontinued. In such refractory cases, Metz et al.[13] recommends repeating the 300-mg dose after 2 weeks.

According to the literature, it is not possible to reduce the dose from 300 mg to 150 mg or to extend the dosing interval to longer than 4 weeks in all patients.[13] This is in line with our findings. Case 1 described above is notably different from the other cases in terms of the treatment regimen because this was our first patient with urticaria and we had only started to gain our own experience.

Duration of remission during omalizumab therapy

Symptoms of urticaria usually recur after 4–8 weeks, although longer periods of remission, lasting even a few months, have been described.[13,15,17]

Interestingly, there are reports of immediate and complete disappearance of severe chronic urticaria after a single dose of omalizumab.[18]

In a study by Metz et al.[13] omalizumab was discontinued every 6–12 months in all patients with a complete remission to assess disease activity. In the majority of patients with CSU and induced urticaria, a remission between the last dose of omalizumab and the development of symptoms lasted from 4 to 8 weeks. On the other hand, one patient with CSU concomitant with pressure urticaria remained asymptomatic for 4 months and two other patients with CSU, for 7 months. Another two patients with CSU and one patient with mixed CSU and solar urticaria did not experience a relapse of symptoms for 4–16 months.[13]

We observed similar findings in our patients; the symptoms gradually recurred within 4–7 weeks after the discontinuation of omalizumab. Importantly, the symptoms resolved on the subsequent

administration of omalizumab, which is clinically significant because patients may experience a few months without any distressing symptoms or side effects related to the long-term use of CSs or other drugs. As an example, one of our female patients achieved a weight reduction of 4 kg over 3 months since the discontinuation of CSs. In addition, numerous symptoms related to the long-term treatment of urticaria resolved, such as drowsiness, depressive and anxiety disorders, and musculoskeletal disorders. Of note, prior to omalizumab therapy, the patient continued to experience symptoms despite the use of a CS, and other types of therapy, including the use of cyclosporine, also proved ineffective.

We did not observe any adverse effects of omalizumab in our patients. The safety of this therapy has also been confirmed by other investigators.[10,11,13,16,17]

Duration of treatment and effect of omalizumab on the natural course of chronic urticaria

There are currently no data indicating that a prolonged use of omalizumab has any disease-modifying properties. So far, omalizumab therapy has been considered as a symptomatic treatment with symptom recurrence within a few weeks. There have been reports of patients who have remained asymptomatic for more than 9 months despite the discontinuation of treatment.[17] Despite the ongoing follow-up of many of those patients, it is still unclear whether the remission has been spontaneous, as is frequently observed in the natural course of urticaria, or whether the drug is particularly effective in a selected group of patients.

Patient selection for omalizumab treatment

Omalizumab may be effective in the treatment of difficult-to-treat CSU, such as in patients who did not achieve a satisfactory control of symptoms with high-dose antihistamine drugs also in combination with antileukotriene drugs. These patients usually require a long-term use of a CS or cyclosporine. Unfortunately, even such therapy is ineffective in a number of patients and is associated with significant adverse effects. In addition, the term "difficult-to-treat chronic urticaria" covers also a group of patients who cannot achieve an adequate control of symptoms using therapies recommended by the current guidelines owing to side effects, as well as a group of patients who fear treatments associated with a risk of severe adverse effects such as a long-term use of CSs or cyclosporine. Omalizumab (Xolair) is currently approved in Poland for use as a supportive treatment of CSU in adult patients and children aged 12 years and older, who do not respond adequately to treatment with H_1 antihistamine drugs.

Use of omalizumab in the treatment of delayed pressure urticaria

DPU and CSU sometimes co-exist in the same patient. The pathogenesis of DPU is still poorly understood. This disease is often refractory to conventional treatments including the use of high-dose nsAHs.

Omalizumab has been described to be useful in patients with DPU and may be an interesting therapeutic option in refractory cases.[13] So far, the efficacy of omalizumab in DPU has not been evaluated in a formal controlled clinical trial. Metz et al.[13] reported that omalizumab was effective in DPU in all investigated patients (seven patients with a complete improvement and one patient with a significant improvement). However, the number of patients with inducible urticaria treated with omalizumab is still too low to draw firm conclusions.[13] Our findings confirm the effectiveness of omalizumab in the treatment of DPU.

The case of a patient with a 20-year history of DPU should be discussed separately. It is a challenging case owing to the persistence of severe symptoms. All the treatment modalities described above were ineffective or had to be discontinued because of adverse effects. The patient was maintained on medium or, at times, high doses of CSs, which only partially alleviated the symptoms of CSU and DPU. After the first administration of omalizumab, the symptoms of CSU resolved within a few days, and the patient could walk outside wearing short-sleeved clothing. However, the symptoms of DPU were not reduced. After the second administration of omalizumab, the patient reported the worsening of symptoms, which required additional doses of CSs. It cannot be excluded that the aggravation of symptoms was related to the natural course of the disease because it was present in the patient's history, especially during summer. We decided to discontinue the treatment because the patient stressed the painful

symptoms of DPU that had not been alleviated. In a study by Nam et al.[19] 10 patients achieved remission at week 4; four at week 12; three at weeks 8 and 16; and one at weeks 20 and 24 (mean total period, 9.27 ± 6.1 weeks).[19] However, because the patient was not convinced as to the effectiveness of this treatment, it was discontinued. Currently, we are monitoring a patient with different types of chronic urticaria, who achieved a clinical improvement and could reduce the use of other drugs (steroid sparing-effect) only after four cycles of omalizumab (we are currently working on a case report).

In summary, the use of omalizumab is undoubtedly a beneficial and effective therapy, which allows to completely resolve the symptoms and significantly reduce the use of other drugs.

Patients with DPU who do not respond to antihistamine drugs and other therapeutic options require particular attention.

Omalizumab: The mechanism of action in urticaria

Although the effectiveness of omalizumab has been studied extensively in chronic urticaria, its mechanism of action remains unclear. It is particularly interesting that a response to omalizumab treatment is quick and complete, which has been confirmed not only by our findings but also those by other authors.[10,11,13] Considering the available data on the action of omalizumab along with the suggestions of various authors, we cannot exclude the IgE-dependent mechanism, at least in a number of patients with various phenotypes of urticarial.[10,11,13]

Omalizumab binds to circulating IgE, regardless of its specificity, to form IgG–IgE complexes, which are incapable of binding to IgE receptors. This process leads to the downregulation of the high-affinity IgE receptor (FcεRI) and reduction of IgE-mediated response.[20,21] Omalizumab causes a rapid decrease in free IgE levels by 96.1% within 3 days and a slower downregulation of the FcεRI on effector cells.[22] It has been demonstrated that the time course for the decrease of FcεRI expression in basophils is faster compared with that in skin mastocytes, occurring within the maximum of 7–14 and 70 days, respectively.[22,23] Therefore, it has been suggested that, in IgE-mediated allergic diseases, omalizumab treatment lasting at least 12–16 weeks is needed before the evaluation of a clinical benefit.[20]

The above mechanism of action explains the effectiveness of omalizumab in IgE-dependent allergic diseases, particularly, in moderate-to-severe asthma or rhinitis. However, the high efficacy of omalizumab in various types of urticaria has not been fully elucidated. In many patients, the benefit of omalizumab treatment was evident as early as within the first few days after the initial dose. This may indicate that there are also other mechanisms of action present or that a wider range of various IgE-mediated processes are involved in the etiopathogenesis of urticaria that have not been described so far. It may be speculated that the formation of IgE antibodies against environmental antigens or IgE-mediated sensitization to autoantigens may be involved in the development of urticarial.[13]

It has been demonstrated that several autoantigens, which are involved in autoimmune diseases, result in the production of IgE autoantibodies.[24] In addition, proteins with a structural similarity to exogenous allergens may cross-react with allergen-specific IgE antibodies. The IgE-reactive autoantigens might induce IgE-dependent effector cell degranulation and induce or augment an inflammatory response in the absence of exogenous allergen exposure.[24] Interestingly, it has been demonstrated that patients with CSU express IgE antibodies against thyroid peroxidase, which could cause "autoallergic" mast cell activation, a novel pathogenesis of CSU.[25]

It has also been demonstrated that the efficacy of omalizumab in DPU was paralleled by a decrease in basophil releasability, suggesting that IgE signaling through the basophil may be involved in the pathogenesis of the disease.[26] A rapid improvement in the symptoms during anti-IgE therapy supports the hypothesis that DPU and CSU might be mediated by the same IgE-dependent mechanism.

After treatment cessation, free IgE levels return to baseline about 18–20 weeks after the administration of the last dose in the majority of patients.[27] In theory, this may explain a gradual symptom recurrence usually 6–8 weeks after the discontinuation of treatment.

Other suggested mechanisms of action of omalizumab include a direct stabilization of effector cells and anti-inflammatory effect of this drug.[13,14] It has also been proposed that omalizumab may

exert some of its effects through direct basophil stabilization[13] or an immunomodulatory mechanism characterized by a reduction in B-cell activation and changes in tumor necrosis factor (TNF)-α, interleukin (IL)-4, and interferon (IFN)-γ synthesis.[28] The most recent studies have shown that a rapid response to omalizumab therapy in chronic urticaria is more likely to result from the elimination of an activating signal, such as IgE, rather than from the generation of a negative inhibitory signal.[29] In addition, it has been demonstrated that omalizumab decreases coagulation activation. Importantly, the effectiveness of both oral anticoagulants and heparin has been observed in some patients with refractory CSU.[10]

Currently, there are no clear indications on the possible factors affecting a response in patients with CSU to the treatment with omalizumab. None of the available studies have shown any association between the response to treatment and the baseline serum IgE levels, the presence of any autoimmune diseases, age and sex of the patients, duration of therapy, or other factors.[10,11,15]

It would be interesting to assess the response to omalizumab in the context of the known markers of CSU severity, including D-dimer.[4,5]

Conclusions

Our findings confirm that omalizumab may be an effective and rapid treatment option in patients with CSU and DPU accompanied by angioedema and refractory to treatment with high-dose H_1 antihistamine drugs. It is important to establish a therapeutic regimen based on the individual patient's needs, in which dosing intervals and duration of the therapy itself are dependent on the type of urticaria. Such an approach might reduce any unnecessary exposure to drugs, adverse drug effects, as well as healthcare costs.

Declaration of Conflicting Interest

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