CASE LETTERS

Urticaria and angioedema as possible reactions of omalizumab*

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Dear editor;

A 55-year-old man presented to our clinic with a 16-year history of chronic spontaneous urticaria (CSU). Given the poor response to H1-antihistamines at high doses alone or in combination with montelukast, he had started to receive omalizumab four months ago (300 mg/SC/every fourth week). He was referred to our clinic because of the exacerbation of his urticaria after this therapy. On physical examination, we detected the continuous eruption of short-lived hives on his body and extremities. He had no angioedema. His urticaria activity score-7 (UAS-7) was 14 in the preceding week. Complete blood count, liver, renal, and thyroid function tests, erythrocyte sedimentation rate, C3-C4 complement levels, and urine analysis were normal. Anti-thyroid and antinuclear antibodies, tests for human immunodeficiency, hepatitis B and C viruses, and stool examinations for parasitic infections were negative. Serum IgE level was 196 IU/mL (normal 0–87), and C-reactive protein (CRP) value was 2.2mg/L (normal<5 mg/L). His chest x-ray and abdominal ultrasonography were normal. Twenty-eight days after the last dose, we administered the fifth dose of omalizumab (300mg/SC) because of the ongoing symptoms. We also thought that the previous exacerbations should not be omalizumab-related. No acute reaction was observed following the administration, but an exaggeration of the urticaria and swelling of the lips and tongue were observed after about 12 hours (Figure 1). The CRP value measured in this period was 10.8mg/L. He was treated with antihistamines and systemic corticosteroids, but the UAS-7 was increased to 39 over the first week (Table 1). In the following period, the patient did not accept the diagnostic tests planned to determine the sensitizing compound of omalizumab.

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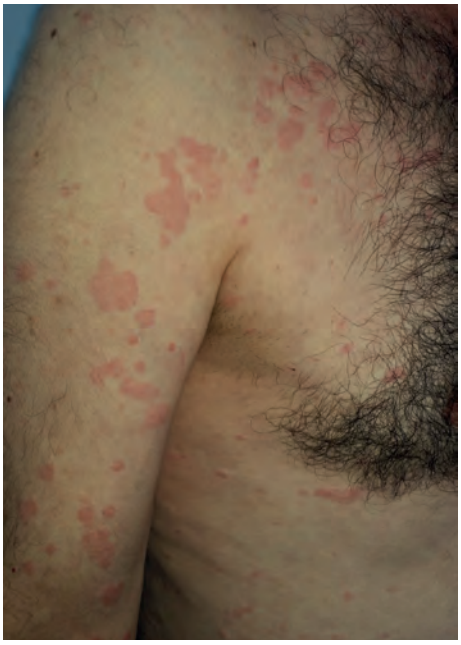

Figure 1: Exacerbation of the urticaria after omalizumab administration in the patient

Table 1: The UAS-7 values of the patient several weeks before and after omalizumab

UAS-7	Before omalizumab	After the 1st dose	After the 2nd dose	After the 3rd dose	After the 4th dose	After the 5th dose
1st week	UN	38	32	32	36	39
2nd week	UN	29	25	24	30	32
3rd week	18	20	21	18	22	26
4th week	16	15	12	13	14	15

UAS: Urticaria Activity Score; UN:Unkown

Omalizumab is a recombinant DNA-derived humanized monoclonal antibody that selectively binds to human IgE. It was originally approved in 2003 for the treatment of persistent allergic asthma, and then was licensed in 2014 for the treatment of patients with antihistamine-refractory CSU. Over the past years, results of clinical studies and practical experience have shown its high efficiency with a rapid onset of action in CSU.[1]

Omalizumab has been known to be associated with serious adverse reactions in patients with allergic asthma, but it has a better tolerability profile in patients with CSU. Most adverse reactions in CSU patients are mild and temporary such as fever, headache, sinusitis and reactions at the injection site.[2] Although the failure of therapy has been rarely mentioned in some reports, exacerbation of urticaria associated with omalizumab is an unusual complication.[3,4] Recently, Ertaş et al. reported four patients with severe antihistamine-resistant CSU, who developed angioedema, anaphylaxis and/or flare-up of urticaria at different times following omalizumab therapy (Table 2).[4] In our patient, the exacerbation of urticaria and

Table 2: Exacerbation of urticaria and angioedema following omalizumab therapy

Patient	Age	Gender	Diagnosis	Disease duration	Omalizumab dosage	Reaction
1*	68y	Male	CSU+ angioedema	4 years	5th	
6th	Angioedema	29	25	24	30	
Urticaria+ angioedema	18	20	21	18	22	
2*	49y	Female	CSU+ angioedema	25 years	2nd	Angioedema
3*	33y	Female	CSU+ angioedema	7 years	1st	
2nd	Hypotension and weakness					
Anaphylaxis						
4*	38y	Male	CSU	5 years	1st	Urticaria
Our patient	55y	Male	CSU	16 years	5th	Urticaria+ angioedema

* Cases in the report of Ertaş *et al*,2016. [4]; CSU: Chronic spontaneous urticaria

development of angioedema after the administration of the drug made us think that it was a paradoxical adverse reaction.

Even though we were not able to make the diagnostic tests, exacerbation of the pre-existing urticaria, and development of angioedema in our patient may be related with the excipients in omalizumab such as polysorbat and histidine rather than the active ingredient. Especially polysorbat is one of the well-established sensitizers that may be involved in the development of severe non-immunological reactions. Anaphylactoid reactions with cutaneous symptoms have also previously been described in asthmatic patients being treated with omalizumab.[5] As most commercial preparations include different excipients which are necessary to preserve and stabilize the product, it should be taken into consideration that these excipients may play a role in the development of such adverse reactions and in unsatisfactory responses to the omalizumab therapy. ❑

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Diphenciprone as a therapeutic alternative to exuberant periungual warts*

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Dear editor,

One of the most frequent diagnoses in a dermatologist's daily practice is viral warts. In many cases, the lesion is self-limiting and frequently resolves without therapeutic intervention – especially in recent cases – with little hyperkeratosis.[1] However, periungual warts, in particular, are frequently associated with high recurrence rates, which poses a therapeutic challenge. Several therapeutic modalities are described in the literature. Some of them include surgical techniques that are sometimes painful and can lead to nail dystrophy. In such cases, physicians can resort to drugs used for immunotherapy with good resolution rates and aesthetic results. In this context, diphencyprone has been studied for some time, with

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