

Rapid response to omalizumab in 3 cases of delayed pressure urticaria



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Clinical Implications

- Delayed pressure urticaria is a rare form of physical urticaria that appears after 4, 6, 8, or even 24 hours in areas exposed to pressure and can lead to a low quality of life.
- Omalizumab should be considered in patients with delayed pressure urticaria unresponsive to conventional treatment.

TO THE EDITOR:

Delayed pressure urticaria (DPU) is a very rare form of physical urticaria. It occurs in approximately 17% of patients with chronic urticaria, and most of the time is associated with chronic spontaneous urticaria (CSU) or other inducible urticaria. In these patients, it is important to identify whether they have DPU and CSU, or whether their CSU is exacerbated by pressure. Symptoms typically appear after 4, 6, 8, or even 24 hours in areas exposed to pressure such as tight clothes, walking or standing up for several hours, sitting down, or sleeping. Laboratory analysis may show leukocytosis with a shift to the left, elevated erythrocyte sedimentation rate (ESR), and elevated C-reactive protein (CRP) level.¹⁻³

Antihistamines are not usually useful and oral corticosteroids work very well, but at high doses, which are unsuitable for long-term treatment. Dapsone, methotrexate, sulfasalazine, anti-TNF- α , or colchicine can be an alternative to corticosteroids. Recently, the use of omalizumab in DPU has been reported.⁴⁻⁶

We present 3 patients, 2 men and 1 woman, with long-term DPU and rapid response to the first dose of omalizumab.

Our first patient is a refinery worker. He wears a safety suit, boots, and helmet during his work time. In the past 4 years, he presented with urticarial lesions on the buttocks and back of thighs, eyelid edema, facial deformity, and dysphagia in acute periods, not related to food or drugs intake. Treatment with antihistamines and leukotriene antagonists was not effective. Cycles of systemic corticosteroids to better control his symptoms were needed. However, symptoms reappeared when steroids were stopped. Except for CRP (Table I), results of all laboratory examinations were normal (hemogramme, biochemistry, hepatic and thyroid function, antibodies against thyroid peroxidase, total IgE, and ESR).

The second patient works standing up in a hardware store for 10 hours a day, and had daily episodes of severe painful hand and foot edema (supporting areas). As a result, he could not wear his shoes when he woke up or handle his cup. He also presented with urticarial lesions on the left side of the body at night (sleeps leaning on that side). He was treated for several years with

antihistamines, leukotriene antagonists, and systemic corticosteroids in high doses, but none was effective. High ESR and CRP level were detected (Table I). Tryptase level was normal (5.43 $\mu\text{g/L}$), and total IgE level was 188 UI/mL.

The third patient is a middle-aged woman, a housewife, with daily symptoms of edema, heat, and pain in her joints (hands, hips, knees, and ankles) without arthritis. As a result of her symptoms, she could not even stir soup with a spoon while cooking, as she would present with symptoms hours later. She was treated with antihistamines, montelukast, colchicine, and cyclosporine without response. Her symptoms could be controlled only by systemic corticosteroids. Her laboratory analyses (blood cell count, biochemistry, hepatic and thyroid function, antibodies against thyroid peroxidase, antinuclear antibody, complement C3, C4, C1 inhibitor, and immunoglobulins G, A, and M) were normal, except for ESR and CRP (Table I). Concomitant rheumatic disease was discarded.

In all 3 patients, their urticaria was recalcitrant and associated with systemic symptoms: slight fever (37.5°C), joint pain, and curiously dysphagia in acute phases, with good responses to systemic corticosteroids in 2 of the 3 subjects and with poor responses in all to antihistamines, leukotriene antagonists, colchicine, and cyclosporine. This led to quality-of-life impairment and limitation in their work and normal life activities such as walking, seating, cooking, or sexual relations. Before omalizumab treatment and during previous treatment regimens, urticaria activity score was noted to be high (see Table I).

To confirm the diagnosis, we performed tests following established protocols using a dermographometer (100 g/m² for 70 seconds on the forearm) and/or suspension of 7-kg weight on their shoulders for 15 minutes. Delayed readings were positive in all 3 patients⁷ (Table I and Figure 1).

After trials with previously cited treatments, we initiated intervention using 300-mg dose of omalizumab every 4 weeks.

After the first dose (300 mg of omalizumab), patients were asymptomatic without further relapse until now. They did not need any other medication to control their symptoms. Two months later, both tests (dermographometer and suspension of 7-kg weight over their shoulder) were repeated and found to be negative.

The etiopathogenesis of DPU is still unclear. Activation of mast cells and different mediators could play a significant role, resembling a late-phase reaction. The typical findings are wheals and/or angioedema in the area in which vertical pressure is applied, but may be associated with constitutional symptoms such as fever, general discomfort, muscle and joint pain, or headache.^{7,8}

Omalizumab binds to circulating IgE to form IgG-IgE complexes. These complexes are not able to bind to IgE receptors. Consequently, there is a downregulation of the high-affinity IgE receptor (Fc ϵ RI), leading to a reduction in IgE-mediated response. The high efficacy of omalizumab in various types of urticaria has not been fully explained. It has been demonstrated that the efficacy of omalizumab in DPU was associated with a decrease in basophil releasability. This suggests that IgE through the basophil may be involved in the pathogenesis of the disease. A rapid response to the symptoms during anti-IgE treatment supports the hypothesis that DPU and CSU might be mediated by the same IgE-dependent mechanism.⁸

TABLE I. Clinical and diagnostic features in our patients

Patient	Sex	Age (y) at diagnosis	Duration of clinical disease (y)	Previous treatment*	UAS-7 before omalizumab	Other associated inducible urticaria	ESR (mm/h)-CRP (mg/dL)	Diagnostic testing/positive-hours/treatment at the moment of diagnosis	UAS-7 after first dose of omalizumab
1	Male	41	>4	1B, 4B, 5A	33 of 42	None	12 mm/h 1.91 mg/dL (0-0.5)	Dermographometer and suspension of 7- kg weight over the shoulder/4-24 h/1B, 5A	0 of 42
2	Male	36	>5	1B, 2A, 3A, 4B, 5A	40 of 42	Dermographism, Cold urticaria	23 mm/h 1.28 mg/dL	Suspension of 7-kg weight over the shoulder/6-24 h/1B, 5A	0 of 42
3	Female	50	>5	1B, 3A, 4B, 5A, 6A, 7A, 8A	39 of 42	None	20 mm/h 2.97 mg/dL	Suspension of 7-kg weight over the shoulder and dermographometer/ 6-8 h/1B, 5A	0 of 42

UAS-7, Urticaria Activity Score.

*1, cetirizine; 2, ebastine; 3, levocetirizine; 4, systemics corticoids; 5, montelukast; 6, raditidine; 7, colchicine; 8, cyclosporine; A, standard dose; B, high dose.



FIGURE 1. Wheals 6 hours after suspension of 7-kg weight over the right shoulder of patient 3.

So far, only 5 cases of DPU and angioedema controlled with omalizumab have been reported in the literature.^{1-4,9}

We and other authors have shown that omalizumab treatment can be safe and effective in patients suffering from recalcitrant inducible urticarias such as DPU.⁹

DPU causes significant impairment in quality of life and its therapeutic management is complex, but fortunately, these 3 patients had a rapid response to treatment with omalizumab after the first dose reaching a Urticaria Activity Score of 0 of 42.

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Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

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